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Volume 28, Number 5 May 1958

CONTENTS

CONTENTS (continued)

CONTENTS (continued)

CONTENTS (continued)

STUDIES IN THE FIELD OF CONJUGATED SYSTEMS

LXXXV. THE CONDENSATION OF DIENE HALIDES WITH ACETYLENE DICARBOXYLIC ESTER*

V. S. Miklashevskaia and A. A. Petrov

Acetylene dicarboxylic acid and its esters are among the most studied of the dienophilic compounds [1]. Among the reactions of these substances with halogen derivatives of the dienes, only the condensation with fluoroprene has been described [2].

In continuation of our studies on the diene synthesis with the participation of diene halides, we have carried out experiments on the condensation of dimethyl acetylene dicarboxylate with some chloro- and bromo-derivatives of divinyl and isoprene.

When we heated acetylene dicarboxylic ester with 1-chlorobutadiene, we could not obtain a definite condensation product.

In the case of 1-bromobutadiene we isolated only phthalic anhydride from the very small yield of a mixture which may or may not have contained halogen compounds. Thus we showed that here condensation proceeds with the splitting out of hydrogen halides. A similar reaction was found earlier when 1-halodienes were heated with ethylene dienophils [3].

Chloroprene and bromoprene gave normal condensation products with acetylene dicarboxylic ester – the dimethyl esters of 4-chloro- and 4-bromo-$\Delta^{1,4}$-dihydrophthalic acid. The first ester was a liquid, the second crystallized on standing.

Attempts to obtain the corresponding chloro- and bromodihydrophthalic acids from these esters by heating with aqueous alkali were unsuccessful. The hydrolysis was accompanied by loss of hydrogen halide and decarboxylation with formation of a mixture of benzoic and halogen containing acids. When esters of 4-fluoro-$\Delta^{1,4}$-dihydrophthalic acid and 4-halo-$\Delta^{1,4}$-dihydrobenzoic acid were saponified no appreciable loss of hydrogen halide and decarboxylation were observed [2,4].

The analogous structures of chloro- and bromoisoprene (3-chloro- and 3-bromo-2-methyl-1,3-butadiene) react with acetylene dicarboxylic ester to form dimethyl esters of 5-chloro- or 5-bromo-4-methyl-$\Delta^{1,4}$-dihydrophthalic acid. Both substances are crystalline. When they were heated with dilute alkali solutions they also lost hydrogen halides and were decarboxylated; in the case of the bromo-ester we isolated p-toluic acid.

EXPERIMENTAL

Condensation with 1-chlorobutadiene.** 0.07 g-mole of 1-chlorobutadiene and 0.07 g-mole of dimethyl acetylene dicarboxylate (1) in 10 ml of toluene were heated in an autoclave at 130-140° for 6 hours. When the reaction product was distilled in a vacuum we obtained 5 g of the starting ester and about 1 ml of a liquid which distilled at 125-130° (10 mm), $n^{20}D$ 1.4993. Chlorine content 8.68%, OCH_3 content 23.14%. The substance was not further studied.

Condensation with 1-bromobutadiene. 0.06 g-mole of 1-bromobutadiene and 0.06 g-mole of ester I in 10 ml of toluene were heated in an autoclave at 160-170° for 14 hours.

Distillation of the mixture in a vacuum gave, besides the starting ester, 3.7 g of an oil boiling at 120-140° (10 mm), from which crystals of phthalic anhydride, m.p. 131°, separated on standing. Mixed m.p. 131°. The

* Diene Compounds. IXIV. The Diene Synthesis with Participation of Diene Halides. X.

** All the diene halides were stabilized with hydroquinone.

formula was confirmed by analysis.

The liquid residue was separated into two fractions: the 1st with b. p. 120-125° (10 mm), $n^{20}D$ 1.5089, contained 18.61% bromine; the 2nd with b. p. 125-130° (10 mm), $n^{20}D$ 1.5179, contained 23.04% bromine. For the expected condensation product we calculated a bromine content of 29.04%, and the boiling point could not be below 140° (10 mm) [2].

Condensation with chloroprene. 0.1 g-mole of chloroprene and 0.1 g-mole of ester I in 20 ml of toluene were heated in a sealed glass tube at 140-150° for 15 hours. We obtained 14.5 g (63%) of dimethyl 4-chloro-$\Delta^{1,4}$-dihydrophthalate.

B. p. 162-163° (10 mm), d^{20}_4 1.2828, $n^{20}D$ 1.5107, MR_D 53.83; calculated 53.42. Found %: Cl 15.58; OCH_3 26.85. $C_{10}H_{11}O_4Cl$. Calculated %: Cl 15.37; OCH_3 26.91.

0.62 g of the substance was heated in a sealed glass tube with a 10% solution of 0.54 g NaOH for 5 hours (to solution) on a boiling water bath. Then the solution was acidified with dilute nitric acid. The resulting precipitate (benzoic acid) was filtered. M. p. 120-121°. A mixed sample with commercial benzoic acid melted at the same temperature. In the filtrate we found 0.0902 g of chlorine which corresponded to 94.5% of the amount in the ester.

In another experiment, 5 g of ester and 2.6 g NaOH (10% solution) were heated under reflux for 5 hours (to solution of the ester). After acidifying with excess sulfuric acid we obtained 1.95 g of a white, crystalline substance with a diffuse melting point (123-165°) and a chlorine content of 9.32% as against 17.51% calculated for the expected acid. From 0.579 g of this mixture we steam-distilled out benzoic acid. The distillate was neutralized with NaOH. We determined 0.1172 g of benzoic acid. After evaporation and acidification we isolated benzoic acid with m. p. 120°.

0.3 g of the mixture was dissolved in 10 ml of ethyl alcohol and passed through a column of aluminum oxide for chromatography. The column of adsorbent was separated into several parts, each of which was treated separately with 0.1 N NaOH solution. The filtered liquid was acidified with sulfuric acid and extracted with ether. Thus, from the upper part of the column we obtained, apparently, 4-chlorodihydrophthalic acid with m. p. 178-181°.

Found %: Cl 16.45. $C_8H_7O_4Cl$. Calculated %: Cl 17.33.

From the lower part of the column we obtained benzoic acid by the same process.

Condensation with bromoprene. 0.1 g-mole of bromoprene and 0.1 g-mole of ester I in 10 ml of toluene were heated in a glass tube at 145° for 15 hours. The reaction product was vacuum distilled. We obtained 14.2 g (52%) of dimethyl 4-bromo-$\Delta^{1,4}$-dihydrophthalate. The substance crystallized on standing.

B. p. 164.5-165.5° (5 mm), m. p. 39-41° (from aqueous alcohol), d^{20}_4 1.4876, $n^{20}D$ 1.5309.

Found %: Br 29.50; OCH_3 22.02. $C_{10}H_{11}O_4Br$. Calculated %: Br 29.04; OCH_3 22.56.

When the ester was saponified, we obtained benzoic acid.

Condensation with 3-chloro-2-methyl-1,3-butadiene. 0.02 g-mole of chloroisoprene and 0.02 g-mole of ester I in 10 ml of toluene were heated in a sealed glass tube at 150° for 12 hours. The reaction product was separated by distillation. It crystallized in the receiver. We obtained 2.4 g (61%) of dimethyl 5-chloro-4-methyl-$\Delta^{1,4}$-dihydrophthalic acid. Colorless tablets with m. p. 69-70° (from methyl alcohol). B.p. 170-171° (10 mm).

Found %: C 54.10, 53.90; H 5.52, 5.53; Cl 14.39, 14.24; OCH_3 24.74; $C_{11}H_{13}O_4Cl$. Calculated %: C 53.99; H 5.36; Cl 14.49; OCH_3 25.37.

Condensation with 3-bromo-2-methyl-1,3-butadiene. 0.07 g-mole of bromoisoprene and 0.07 g-mole of ester I in 10 ml of toluene were heated in a sealed tube at 140-150° for 12 hours. We obtained 15.7 g (77%) of dimethyl 5-bromo-4-methyl-$\Delta^{1,4}$-dihydrophthalate. Colorless needles with m. p. 73-73.5° (from methyl alcohol). B. p. 154-155° (about 3 mm).

Found %: C 46.08, 46.11; H 4.28, 4.46; Br 27.38; OCH_3 21.93. $C_{11}H_{13}O_4Br$. Calculated %: C 45.69; H 4.53; Br 27.64; OCH_3 21.47.

In various experiments on the hydrolysis of this ester by heating it with a 10% solution of NaOH, the

content of bromide ion in the solution reached 99% of the total in the ester sample. From the hydrolytic product we isolated p-toluic acid (yield up to 60%). M. p. 178° (from water). A mixed test with commercial p-toluic acid melted at the same temperature.

SUMMARY

1. We have studied the condensation of the dimethyl ester of acetylene dicarboxylic acid with 1-chloro- and 1-bromobutadiene, chloroprene, bromoprene, and 3-chloro- and 3-bromoisoprene.

2. In the case of the last four substances we have isolated and characterized the expected condensation products – the dimethyl esters of the corresponding halodihydrophthalic acids.

3. Phthalic anhydride was isolated from the condensation product of acetylenedicarboxylic ester with 1-bromobutadiene.

4. We have shown that the esters of 4-halodihydrophthalic acids and their homologs lose hydrogen halides and are decarboxylated when they are heated with alkali solutions.

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STUDIES IN THE FIELD OF CONJUGATED SYSTEMS

LXXXVI. THE COMBINATION OF PIPERYLENE HYDROCHLORIDE WITH ISOPRENE*

A. A. Petrov, N. A. Razumova, and M. L. Genusov

It was shown earlier that diene hydrocarbons react with halogen compounds in the presence of a catalyst, zinc chloride, tin chloride and others, with formation of a mixture of substances of the general formula $R-(C_nH_{2n-2})_x-X$ [1, 2]. Only saturated halogen compounds were thoroughly studied; it was shown that the rate of the reaction and the size of x depend on the nature of the alkyl halide and the structure of the diolefin. The simplest products of the combination (when x = 1) were isolated only in the case of tertiary alkyl halides and divinyl.

The investigation was continued with the study of the reaction of diene hydrocarbons with unsaturated halogen compounds of the allyl type. There was evidence in the literature of the combination of divinyl and crotyl chloride and bromide with the formation of chlorooctadienes and higher telomers [2]. We showed in our laboratory that prenyl chloride (1,4-isoprene hydrochloride) combined with isoprene to form geranyl chloride and other products [3].

In the present paper we give the results of our experiments on the combination of piperylene hydrochloride (2-chloro-3-pentene) with isoprene.

Piperylene hydrochloride is favorably distinguished from the hydrochlorides of other very simple diene hydrocarbons by the fact that both allyl isomers here have the same structure. This peculiarity of piperylene hydrochloride excludes the possibility of the participation of two isomeric forms of the hydrochloride in the reaction with the diene hydrocarbon and, hence, reduces doubly the number of possible isomeric products of the combination. The diene hydrocarbon, too, was not chosen by chance. As a result of the combination of the above hydrochloride with isoprene in the 1,4-position, we should obtain an isomer of geranyl chloride from which it would be possible to go to isomers of citral, pseudoionone, and ionone which would have practical interest.

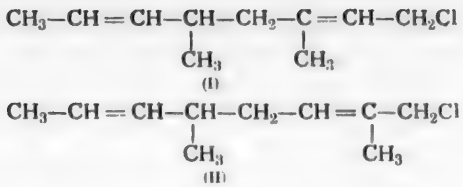
Our experiments on the combination of 2-chloro-3-pentene and isoprene showed that the reaction proceeds in the usual way with formation of a mixture of telomers; the relative yield of the primary product of combination (at x = 1) depends chiefly on the time of contact of the reagents and the catalyst, that is, on the depth of the telomerization process. When 80% isoprene is used, the primary product of the combination and higher telomers (including dimeric halogen compounds) are obtained in a weight ratio of 1:1; when 50-35% of the isoprene is used, in a ratio of 2.5:1. However, in all these cases, the initial combination product forms in considerably greater quantity than, for example, in the reaction of prenyl chloride with isoprene.

We studied only the products of combination of piperylene hydrochloride and isoprene in 1:1 ratio. As a result of the combination of 2-chloro-3-pentene and isoprene it was possible to isolate 6 isomers with open chains and two cyclic compounds.

The actual combination products were distilled at low temperatures. The structure of the main part was established from the following data.

1) 85% of the substance reacted with formation of an aldehyde isomeric with citral in the Sommelet reaction [4]. Hence 85% of it is a primary chloride of the allyl type. The aldehyde can be obtained only from two possible products of combination of 4-chloro-2-pentene and isoprene in the 1,4- and the 4,1-positions.

*Diene Compounds. LXV. Reaction of Dienes with Halogen Compounds. III.

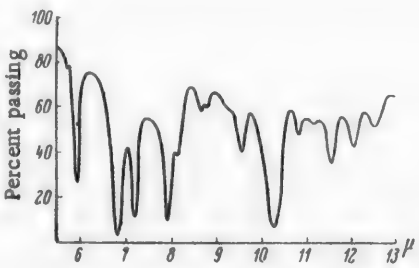


(I)

(II)

2) When the substance is split by ozone it gives acetic, chloroacetic, and methyl levulinic acids. Chloroacetone was not found. Hence formula II is excluded and there remains only formula I.

3) On hydrogenation over palladium the compound gives a saturated hydrocarbon, evidently 3,5-dimethyloctane. According to the specific gravity and refractive index it hardly differs from the form described in the literature but it has a somewhat unsharp boiling point range (2°).



Infrared spectrum of the chief fraction (NaCl prism, thickness of layer 0.1 mm).

4) The infrared spectrum of the substance (about 1.6μ and in the interval 5.5-13μ) also confirms formula I. In the spectrum there is a very intense absorption band at 970 cm^{-1}, which corresponds to the grouping —CH=CH—, and a less intense band at 864 cm^{-1} which evidently corresponds to the group $R_2C{=}CH{-}$. A double bond is characterized by the frequency 1669 cm^{-1} which evidently occurs because of the summation of the frequencies which lie close together and come from the two internal double bonds. The frequency 922 cm^{-1} which can be related to the group $CH_2{=}$ appears weakly in the spectrum of the starting substance. Notable absorption characteristic of this group is also absent at 6100 cm^{-1}. On the other hand, after the Sommelet reaction, the spectrum of the result shows intense absorption at 906, 970, and 6100 cm^{-1}, characteristic for the vinyl group [5]. Hence this substance contains the product of combination of 2-chloro-3-pentene in the 1,2-position.

Thus we have shown that isoprene unites with 2-chloro-3-pentene preferably in the 1,4-position, with formation of 1-chloro-3,5-dimethylocta-2,6-diene. The 1,2-product is formed to the extent of less than 15% of the mixture of substances with the formula $C_{10}H_{17}Cl$.

This investigation has made available the above isomer of geranyl chloride, and also the isomer of citral, 3,5-dimethylocta-2,6-dienal, not previously described in the literature. The latter is a colorless oil with an odor resembling that of citral. It reacts easily with hydrazine derivatives: it gives a crystalline semicarbazone and 2,4-dinitrophenylhydrazone. When it condenses with acetone it gives an isomer of pseudoionone, 6,8-dimethylundeca-3,5,9-trien-2-one.

EXPERIMENTAL

Piperylene hydrochloride was obtained by saturating piperylene (a mixture of cis- and trans-forms with $n^{20}D$ 1.4334) with hydrogen chloride at 0° to a weight which corresponded to about 50% conversion. The hydrochloride was purified by vacuum distillation in a Widmer column (80 mm). The yield was about 95% based on the hydrogen chloride absorbed.

B. p. 41° (100 mm), 45-46° (120 mm), d^{20}_4 0.3994, $n^{20}D$ 1.4327. These constants correspond to the literature data for 4-chloro-2-pentene [6].

Telomerization was carried out in a special apparatus which allowed determination of the specific gravity of the mixture during the reaction. To a mixture of equimolecular amounts of piperylene hydrochloride and isoprene diluted with 25-50% of the weight with methylene chloride was added at 10° a 5% solution of tin chloride in methylene chloride, and the mixture was stirred at the same temperature until there was no further increase

in specific gravity (determined experimentally) beyond a set value which showed that a determined depth of reaction had been reached. Then the reaction was stopped by adding diethylamine [7] and the mixture was distilled. The fraction of primary combination product was collected at 70-100° (10 mm). Under these conditions we carried out a series of experiments, some of which are described below.

a) We took 34 g (0.5 g-mole) of isoprene, 52 g (0.5 g-mole) of hydrochloride, and 30 ml of methylene chloride. We added 3 ml of 5% tin chloride solution. After the specific gravity had increased by 0.043, which took about 20 minutes, the reaction was stopped by adding 1.5 ml of diethylamine. We obtained 14.5 g of primary product and 6 g of higher telomers (including also dimers of the halogen derivatives). The depth of the transformation was about 35%.

b) With the same amounts of starting substances with an increase in specific gravity of 0.060 we obtained 27 g of primary product and 11 g of telomers. The depth of transformation was about 50%.

c) Under analogous conditions with an increase in specific gravity of 0.104 we obtained 36 g of primary product and 32 g of higher telomers. The depth of transformation was about 80%.

The primary combination products from several experiments were distilled in the Widmer column. The chief fraction (within 1°, chiefly 1-chloro-3,5-dimethylocta-2,6-diene) made up about 80% of the whole mixture. For this fraction we found:

B. p. about 64° (3 mm), 85-86° (10 mm), d^{20}_4 0.9132, $n^{20}D$ 1.4730, MR 53.05; calculated 52.31. Found %: C 69.75, 69.88; H 9.94, 10.11; Cl 20.38. $C_{10}H_{17}Cl$. Calculated %: C 69.55; H 9.92; Cl 20.53.

Ozonization. 5.28 g of the substance was ozonized in ethyl chloride until absorption of ozone stopped. After the solvent was evaporated, the ozonide was decomposed by heating it with a solution of hydrogen peroxide. The decomposition product was extracted with ether in an extractor with a stirrer. When the ether extract was distilled we obtained acetic acid (30-48° at 30 mm), chloroacetic acid (68-72° at 10 mm), and methyl levulinic acid (about 135° at 9 mm).

Acetic acid was transformed into the anilide by the action of the calculated amount of thionyl chloride and then aniline. M. p. 113° (from water). A mixed melting point with a commercial sample of acetaniiide showed no depression. Chloroacetic acid was isolated in the crystalline state, washed with petroleum ether, and recrystallized from the same solvent. M. p. 61-62°, confirmed by mixed melting point. Methyl levulinic acid was converted to the semicarbazone, m. p. 180-181° (from water) [8], and the 2,4-dinitrophenylhydrazone, m.p. 188-188.5° (from alcohol), which were analyzed.

Semicarbazone. Found %: N 22.78, 22.87. $C_7H_{13}O_3N_3$. Calculated %: N 22.45.

2,4-Dinitrophenylhydrazone. Found %: N 18.19, 18.24. $C_{12}H_{14}O_6N_4$. Calculated %: N 18.06.

Sommelet reaction. A preliminary determination in a small sample of the chief fraction by the method of [9] showed about 85% of primary chloride.

Then 15 g of hydrochloride in 75 ml of methylene chloride was mixed and boiled with 15 g of dry urotropin during 7 hours. The urotropin complex was extracted with two portions of water. The methylene chloride solution was separated, dried, and again treated with 10 g of urotropin for 6 hours, and then washed with water. After the methylene chloride was evaporated in a vacuum, we obtained a total of 1.5 g of residue. The water solutions of the urotropin complex were combined and gradually added to a solution of formalin with simultaneous steam distillation. The aldehyde was removed from the distillate by ether. We obtained 7.5 g (57%) of 3,5-dimethylocta-2,6-dienal.

If the reaction was carried out with urotropin by vibration in the cold for two days, the yield did not change.

B. p. 110-111° (20 mm), d^{20}_4 0.8786, $n^{20}D$ 1.4830, MR 49.39 calculated 47.46.

Found %: C 79.06, 78.84; H 10.88; 10.75. $C_{10}H_{16}O$. Calculated %: C 78.90; H 10.60.

Semicarbazone: m. p. 150° (from water). White crystals.

Found %: N 19.98, 19.95. $C_{11}H_{19}ON_3$. Calculated %: N 16.86

2,4-Dinitrophenylhydrazone: orange crystals. M. p. 107° (from alcohol).

Found %: N 16.78, 16.71. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.86.

The residue after the Sommelet reaction had the following properties:

B. p. 70-86° (10 mm), d^{20}_4 0.9220, $n^{20}D$ 1.4670; contained 11.5% hydrolyzed chlorine and about 76% diene compound (Kaufman method).

17 g of 3,5-dimethylocta-2,6-dienal, 32 g of acetone, and 33 ml of 10% solution of Na_2SO_3 were shaken in the cold for 75 hours. By vacuum distillation we obtained 14.5 g (67.5%) of a product with b. p. 139-142° (10 mm). The residue weighed 2.3 g.

6,8-Dimethylundeca-3,5,9-trien-2-one had the following constants:

B. p. 140-141° (10 mm), d^{20}_4 0.8888, $n^{20}D$ 1.5278, MR_D 66.62; calculated 60.84.

Found %: C 81.30, 81.23; H 10.80, 10.74. $C_{13}H_{20}O$. Calculated %: C 81.19; H 10.48.

The semicarbazone, obtained in the usual way, had a m. p. 174-175° (from 50% alcohol).

Found %: N 16.68. $C_{14}H_{23}ON_3$. Calculated %: N 16.85.

Hydrogenation. 10 g of the chief fraction in 100 ml of methyl alcohol was hydrogenated in the presence of 40 g of palladium catalyst on calcium carbonate (with a content of 0.012 g of palladium per g of catalyst) [10]. There was absorption of 3520 ml of hydrogen (755 mm, 20°) which was 82.4% of the calculated amount. The mixture was distilled with steam. We found about 95% of the total chlorine in the sample in the residue. The distillate was diluted with a saturated $CaCl_2$ solution (to remove methyl alcohol). The hydrocarbon layer was separated, washed with a saturated $CaCl_2$ solution, a solution of potassium permanganate (to remove unsaturated hydrocarbons), dried over $CaCl_2$, and distilled in a small Widmer column. We obtained 6 g (59%) of 3,5-dimethyloctane.

B. p. 158-160°, d^{20}_4 0.7151, $n^{20}D$ 1.4132.

Literature data [11]: b. p. 160°, d^{20}_4 0.7136, $n^{20}D$ 1.4130.

SUMMARY

1. We have studied the reaction of telomerization between piperylene hydrochloride (2-chloro-3-pentene) and isoprene in the presence of tin chloride.

2. We have shown that combination occurs chiefly in the 1,4-position, and the primary product of the reaction is preferentially 1-chloro-3,5-dimethylocta-2,6-diene.

3. The latter substance gives by the Sommelet reaction an isomer of citral: 3,5-dimethylocta-2,6-dienal. We have described its crystalline semicarbazone and 2,4-dinitrophenylhydrazone. Condensation with acetone gives an isomer of pseudoionone.

4. We have shown that hydrogenation over palladium transforms the chlorodimethyloctadiene into 3,5-dimethyloctane.

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ACETYLENE DERIVATIVES

192. THE STEREOCHEMISTRY OF HYDROGENATION OF ACETYLENIC GLYCOLS

I. N. Nazarov*, L. D. Bergel'son, L. P. Badenkova and B. V. Lopatin**

Catalytic hydrogenation of acetylenic compounds is known to lead mainly to cis-olefins [1]. It has been often observed, however, that trans-isomers are formed at the same time, and the relative amounts appear to depend on the nature of the acetylenic compound and catalyst, and on the conditions of hydrogenation [2-14].

In connection with our investigations of the stereochemistry of addition reactions at the triple bond, it was of interest to make precise determinations of the quantities of trans-olefins formed in catalytic hydrogenation of disubstituted acetylenes and to establish whether cis-olefins undergo isomerization under hydrogenation conditions. We selected tetramethylbutynediol (2,5-dimethyl-3-hexyne-2,5-diol) and butynediol as compounds for investigation.

Stereochemistry of hydrogenation of tetramethylbutynediol. The main product of hydrogenation of tetramethylbutynediol over Pd catalyst is cis-tetramethylbutenediol with m. p. 69° [15]. The question of formation of trans-tetramethylbutenediol has hitherto remained obscure.

Zal'kind [16,17] isolated a substance with m. p. 75-76° during catalytic hydrogenation of tetramethylbutynediol; he first considered this to be the cis-isomer, but later the trans-isomer. Bourguel [10,11] assumed that the substance with m. p. 75-76° is a mixture of cis-form and "trans-isomer" which did not give a depression of melting point with the compound with m. p. 101° obtained by reduction of tetramethylbutynediol with sodium in alcohol. Later, however, Zal'kind and Bukhovets [18] established that Bourguel's "trans-form" with m. p. 101° gives a dibromide identical with the dibromide of the acetylenic glycol and breaks down with formation of acetylene when heated with caustic alkali. They therefore concluded that Bourguel's substance is a crystalline modification of tetramethylbutynediol (m. p. 95°). Data of the different authors for the geometrical isomers of tetramethylbutenediol are presented in the following table.

Melting Points			Literature
69°	75-76°	101°	
Trans	Cis	–	[19]
Cis	Trans	–	[20]
Cis	Trans-cis mixture	Trans	[10,11]
Cis	Trans	Acetylenic glycol	[18] [21]
Cis	Trans-cis mixture	Acetylenic glycol	[22]

For the purpose of evaluating these conflicting data, it was necessary to obtain authentic specimens of pure cis- and trans-isomers of tetramethylbutenediol. We synthesized these substances from the dimethyl esters of maleic and fumaric acids.

* Deceased.

** B. V. Lopatin carried out the stereographic part of the work.

Condensation of maleic ester with methyl magnesium bromide was effected in 1940 by Johnson [21, 22] who showed that cis-tetramethylbutenediol (m. p. 69°) was formed together with a considerable amount of the product of 1,4-addition. Johnson was unable to effect a similar condensation with fumaric ester because methyl magnesium bromide adds on to fumaric ester only in the 1,4-position even at -40°. Similar results had been obtained even earlier in a study of the reaction of fumaric ester with phenyl magnesium bromide [23].

We found that 1,4-addition can be partly prevented by the use of methyl magnesium chloride. With this reagent we obtained cis-tetramethylbutenediol with m. p. 69° from maleic ester, and trans-tetramethylbutenediol with m. p. 95-96° from fumaric ester. The latter was therefore different from all of the preparations previously assumed to be the trans-isomer. Trans-tetramethylbutenediol can be prepared by reduction of tetramethylbutynediol with lithium in liquid ammonia.

It remained to clarify the nature of the substances with m. p. 75-76° and 101° isolated by Zal'kind and Bourguel.

Bourguel's results [10,11] indicated the possibility of Zal'kind's "trans-form" with m. p. 76° actually being a molecular compound of the cis- and trans-forms. We found that a substance with m. p. 75° is easily formed when solutions of the pure cis- and trans-tetramethylbutenediols in ether are mixed. During recrystallization from ligroine it behaves like an individual compound; nevertheless, it could be resolved into the cis- and trans-forms by crystallization from water, and the pure cis-isomer is eluted (yield about 70%) by chromatography with ligroine on alumina.

The infrared spectrum of the molecular compound with m. p. 75-77° (in carbon tetrachloride) contains strong absorption bands of the associated hydroxyl groups (at 3460 cm^{-1}), but the bands of nonassociated hydroxyls (in the 3600 cm^{-1} region) are nearly completely absent (see Fig. 1). These observations show that the complex is either a long chain of associated molecules (not fewer than ten) joined by a hydrogen bond, or consists of a cyclic structure. Comparison of the relative intensity of the bands of the cis- and trans-olefinic compounds (in the 1600 cm^{-1} region), as well as data obtained during its resolution into the components, show that it contains 1 molecule of trans-tetramethylbutenediol for every 3 molecules of cis-isomer. The cis- and trans-tetramethylbutenediols are very firmly combined in the complex, as is confirmed by the presence of a very strong band of the associated hydroxyl groups even in very dilute solutions (1:10,000 in carbon tetrachloride).

Bourguel's "trans-isomer" (m. p. 101°) was likewise found to be heterogeneous. We found that this substance is formed in quantitative yields when ethereal solutions of tetramethylbutynediol (m. p. 95°) and trans-tetramethylbutenediol (m. p. 95-96°) are mixed in 1:1 ratio. Approximately the same composition of the complex is indicated by comparison of the intensity of the bands at 1662 and 1453 cm^{-1} in the infrared spectra of the complex and of pure trans-tetramethylbutenediol (see Figs. 2 and 3). We see that reduction of tetramethylbutynediol under Bourguel's conditions (sodium in alcohol) does not go to completion, and we can now understand why Zal'kind succeeded in converting Bourguel's "trans-form" into an acetylenic glycol derivative.

Having obtained a supply of pure cis- and trans-isomers of tetramethylbutenediol, we were able to proceed to a study of the stereochemistry of the hydrogenation of tetramethylbutynediol.

During hydrogenation of tetramethylbutynediol over Pd/$CaCO_3$ the rate of uptake of hydrogen falls off sharply after addition of the first molecule of hydrogen (see Fig. 5).

The resulting product does not contain tetramethylbutynediol, since when heated with alkali it does not release acetylene or dimethylethynyl carbinol. Its quantitative resolution into cis- and trans-isomers by fractional crystallization and by chromatography is difficult due to the relatively small quantity of trans-isomer and the loss during recrystallization. The composition of the hydrogenated mixture was therefore determined spectrographically. As had been expected, the infrared spectrum of trans-tetramethylbutenediol contains characteristic absorption bands (at 968 and 1634 cm^{-1}) which are absent from the spectrum of the cis-isomer. It was impossible to directly calculate the concentrations of components in their mixture on the basis of the intensity of these bands, since a study of specially prepared mixtures of authentic composition showed that the spectra of the mixtures appreciably deviate from the Lambert-Beer law due to the formation of the molecular complex. It was therefore decided to construct calibration curves based on the intensity of the absorption bands of four mixtures of known composition (see Fig. 4). The calibration curves were plotted for the 1600 and 1400 cm^{-1} regions (the plot for the 900 cm^{-1} region did not give a smooth curve). Data obtained with the help of these

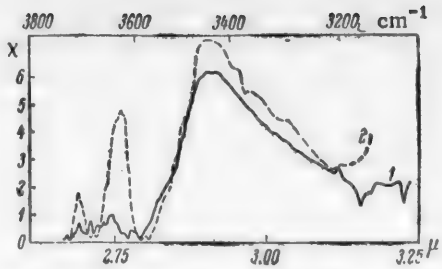


Fig. 1. Absorption spectra. 1) molecular complex of cis- and trans-tetramethylbutenediols (m. p. 75°) in the 3600-3200 cm^{-1} region in CCl_4 at a concentration of 0.0032 g/100 ml; 2) artificially prepared mixture of cis- and trans-tetramethylbutenediols of authentic composition (17:3) in CCl_4 at a concentration of 0.09 g/100 ml.

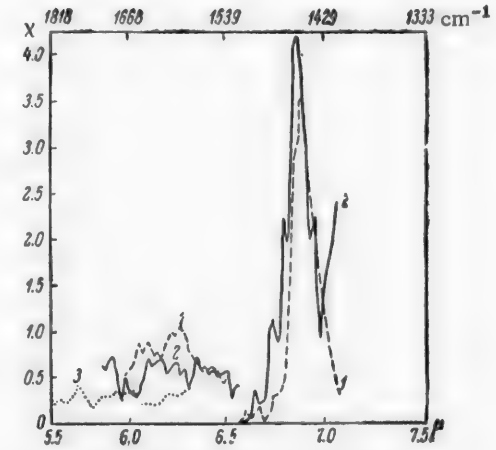


Fig. 2. Absorption spectra of cis- and trans-tetramethylbutenediols and of trans-butenediol in the 1600 cm^{-1} region. 1) trans-tetramethylbutenediol in chloroform; 2) cis-tetramethylbutenediol in chloroform; 3) trans-butenediol in dioxane.

graphs showed that the product of hydrogenation of tetramethylbutynediol over Pd/$CaCO_3$ contains 84-88% of cis-tetramethylbutenediol and 12-14% of the trans-form. Since the calibration curve deviates considerably from linearity, the relative error of measurement by this method is rather large. A check on a similar mixture of known composition indicated a relative error of about 30%. The mean content of trans-tetramethylbutenediol in the hydrogenated mixture is therefore 13 ± 4%.

Stereochemistry of the hydrogenation of butynediol. Although the hydrogenation of butynediol has been realized on the industrial scale [24], the stereochemistry of this reaction has not been closely investigated. Romanet [2] established by fractional distillation that the product of hydrogenation of butynediol over skeletal nickel contains a considerable quantity of trans-butenediol, amounting in one case to 30%. Its content varies considerably, however, from experiment to experiment, and these results could not be reproduced. The literature is lacking in any data for the steric composition of the product of hydrogenation of butynediol over Pd catalyst. Since the stereoisomeric butenediols are liquids (the trans-isomer melts at 25°) and boil fairly closely, it appeared expedient to study the composition of the product of hydrogenation of butynediol by the spectral method. We first attempted to prepare the pure cis- and trans-butenediols needed for this determination by reduction of the dimethyl esters of maleic and fumaric acids with lithium aluminum hydride. The only product that could be isolated from this reaction, however, was saturated 1,4-butanediol. We therefore limited ourselves to the preparation in the pure form of trans-butenediol, which was synthesized by Valette's method [25] from butadiene via trans-1,4-dibromo-2-butene.

The infrared spectrum of the product of partial hydrogenation of the butynediol (absence of the band of the triple bond from the 2500-1700 cm^{-1} region) shows that the first mole of hydrogen adds on to the acetylenic bond just as selectively as in the case of tetramethylbutynediol. There is a considerable difference, however, between the speeds of hydrogenation of the two acetylenic glycols. In tetramethylbutynediol the triple bond is hydrogenated very much faster that the double bond, whereas in butynediol the hydrogenation speeds up after absorption of the first mole of hydrogen (see Fig. 5). Butynediol thus behaves like acetylene, which is hydrogenated over Pd catalyst more slowly than ethylene [26].

This difference in the behaviors of butynediol and tetramethylbutynediol is probably due to steric factors. Both in butynediol and tetramethylbutynediol the triple bond is sufficiently open to allow the molecule to come close up to the catalyst. After the acetylenic derivative has been converted into an olefinic one, further hydrogenation of the molecule depends upon its approach to the catalyst from the side of a plane perpendicular to the plane of the π-bond. Inspection of models shows that such an approach is not hindered in any way in the case of ethylene and butenediol, whereas the methyl groups constitute a hindrance in the case of tetramethylbutenediol. The relatively faster absorption of the first mole of hydrogen by tetramethylbutynediol in comparison with butynediol is presumably due to the inductive effect of the methyl groups which activate the triple bond. Such an inductive effect is clearly observable in the hydrogenation of di-(p-tolyl)-butynediol, which takes up hydrogen

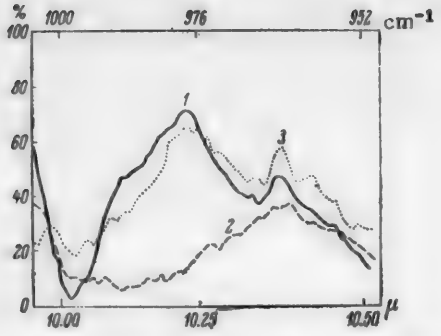


Fig. 3. Absorption spectra of cis- and trans-tetramethylbutenediols and of trans-butenediol in the 900 cm^{-1} region: 1) trans-tetramethylbutenediol in chloroform; 2) cis-tetramethylbutenediol in chloroform; 3) trans-butenediol in dioxane.

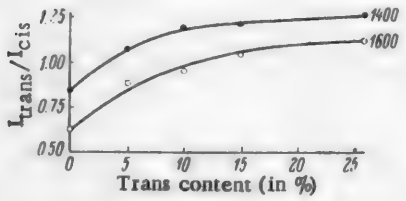


Fig. 4. Calibration graph for determination of the content of cis- and trans-tetramethylbutenediols in mixtures.

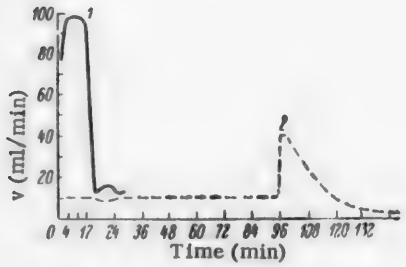


Fig. 5. Rates of hydrogenation of tetramethylbutynediol (3.32 g) and butynediol (2 g) in methanol over 10% Pd/ $CaCO_3$: 1) tetramethylbutynediol; 2) butynediol.

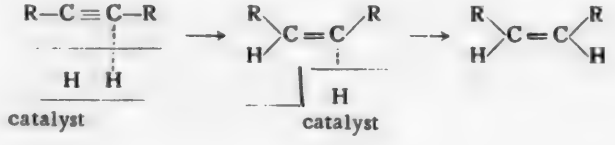
several times faster than diphenylbutynediol [27].

Another characteristic of butynediol is that its hydrogenation over Pd/ $CaCO_3$ is accompanied by formation of a resin (up to 15% of the original butynediol) whereas tetramethylbutynediol scarcely resinfies under the same conditions. At first we assumed that resinification is the consequence of isomerization of butenediol to γ-hydroxybutyraldehyde, since the patent literature indicates the possibility of such an isomerization over Pd catalyst at elevated temperature [28]. This theory had to be abandoned, however, when it was found that a still greater quantity of resin is formed on hydrogenation of butynediol diacetate. Judging by the good solubility of the resin in polar organic solvents, it is a product of partial condensation of the diacetate. By extraction with alcohol we isolated from it the dimer of butenediol diacetate with m. p. 104-105°, which had been described by Raphael [29].

Judging by the curves of the infrared spectra of pure trans-butenediol and of the product of hydrogenation of butynediol, the isomeric butenediols do not give a molecular complex similar to the complex of the stereoisomeric tetramethylbutenediols. The content of trans-butenediol in the hydrogenated mixture was therefore determined in the usual manner according to the Lambert-Beer law, on the basis of the intensities of the absorption bands at 1600 and 900 cm^{-1} which are characteristic of the trans-ethylenic bond (see Figs. 2 and 3). On the basis of the first of these bands the content of trans-butenediol was 19%; on the basis of the second band it was 17%. A check of the accuracy of the method of determination, carried out on an enriched mixture to which a known quantity of trans-isomer had been added, showed that the relative error can be as much as 30%. Consequently, the hydrogenated mixture has an average content of 18 ±6% of trans-isomer. In spite of the serious experimental error, these data show that hydrogenation of butynediol gives more trans-isomer than in the case of tetramethylbutynediol. Therefore all of the preparations of butenediol which had previously been regarded as the cis-form [24, 25, 30] are actually mixtures of cis- and trans-isomers.

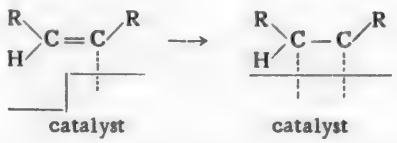
A still larger quantity of trans-form is obtained on hydrogenation of butynediol diacetate. Spectral analysis revealed a content of about 30% of trans-isomer in the product of hydrogenation.

Mechanism of formation of trans-olefinic compounds on hydrogenation. In the hydrogenation of acetylenes the semihydrogenated form does not possess free rotation, and the second hydrogen atom must add on in the cis-position.



Some authors have suggested that the trans-isomer is formed by isomerization of the cis-form in presence of the catalyst (see review [1]). Such an isomerization has never been experimentally realized (at low temperatures). It does not seem probable, since reversible isomerization must involve an equilibrium shift in the direction of the trans-form, but the quantity of trans-isomer is always small.

In connection with the hypothesis of isomerization of the cis-form, we studied the behavior of cis-tetramethylbutenediol under the conditions of hydrogenation of the triple bond. For this purpose we made use of poisoned Lindlar catalyst[31]which, as is well known, selectively reduces the triple bond to double, but is incapable of effecting hydrogenation of the olefinic bond. Cis-tetramethylbutenediol was found to be completely unchanged when shaken for a long period with this catalyst in a hydrogen atmosphere. Therefore in hydrogenation in presence of Pd catalyst the trans-glycols are not formed by isomerization of cis-butenediols. It is more probable that trans-glycols are formed in the actual hydrogenation process due to isomerization of a small portion of the semihydrogenated form at the radical with free rotation.



The free radical can be stabilized by dimerization or by polymerization, or again by transition to the trans-form.

The existence of such free radicals during hydrogenation of acetylene and methylacetylene [32] has been postulated on the evidence of formation of polymers at the same time as olefins. Formation of relatively large quantities of polymers during the hydrogenation of acetylenic glycols supports the hypothesis of the existence of a radical form of the semihydrogenated complex. In this connection it is characteristic that the quantity of trans-form increases at the same time as the quantity of polymers in the following order: tetramethylbutynediol, butynediol, butynediol diacetate.

It is reported in the literature that when acetylenes are hydrogenated with Pd catalyst poisoned by quinoline, the quantity of trans-olefin is greater than when hydrogenation is performed with unpoisoned catalyst [14]. It has even been claimed that the amount of trans-isomer depends upon the proportion of quinoline [33]. We checked these claims in a series of experiments in which tetramethylbutynediol was hydrogenated over Pd/ $CaCO_3$ in presence of various quantities of quinoline. Spectral analysis showed that the composition of mixtures of tetramethylbutenediols formed under these conditions hardly differed from that of mixtures hydrogenated with unpoisoned catalyst.

EXPERIMENTAL

Preparation of cis-tetramethylbutenediol from dimethyl maleate. A solution of 5 g of dimethyl maleate in 50 ml of absolute ether was added dropwise in the course of 2 hours, with stirring and ice-cooling, to an ethereal solution of methyl magnesium chloride prepared from 9.8 g of magnesium and 250 ml of absolute ether. The white precipitate was decomposed with saturated ammonium chloride solution. The ether layer was separated and the aqueous layer extracted with ether; the combined ethereal solutions were dried with magnesium sulfate. The ether was driven off, and the residual oil (3 g) deposited crystals when cooled; after recrystallization from ligroine (b. p. 40-60°) the crystals melted at 68-70°. Yield 0.66 g.

Fractionation of the mother liquor gave two fractions: 1st, b. p. 33.5-34° (40 mm) and 2nd, b. p. 125-140° (40 mm), $n^{21}D$ 1.4510. Freezing of the 2nd fraction (1.87 g) led to deposition of crystals with m. p. 68-69° (from ligroine). Yield 0.63 g. Total yield of cis-tetramethylbutenediol 1.3 g (15%).

Found %: C 66.33, 66.38; H 10.97, 11.16. $C_{18}H_{14}O_2$. Calculated %: C 66.62; H 11.18.

Preparation of trans-tetramethylbutenediol. a) From dimethyl fumarate. 8 g of dimethyl fumarate was condensed with methyl magnesium chloride under the same conditions as for dimethyl maleate. The reaction mixture was worked up to give two fractions: 1st with b. p. 45-100° (6-7 mm), $n^{20}D$ 1.4503; 2nd with b. p. 100-120° (1 mm), $n^{20}D$ 1.4631.

Crystals (0.65 g) came down from the 1st fraction on standing in a refrigerator; after being washed with ligroine and isooctane, they melted at 95-96°. Yield of pure trans-tetramethylbutenediol 0.5 g.

Found %: C 66.67, 66.90; H 11.06, 11.02. $C_8H_{14}O_2$. Calculated %: C 66.62; H 11.18.

b) By reduction of tetramethylbutynediol with sodium in liquid ammonia. 12 g (0.5 mole) of sodium was dissolved in 300 ml of liquid ammonia. A solution of 20 g (0.14 mole) of tetramethylbutynediol (m. p. 94.5-95.5°) in 30 g of anhydrous alcohol was then added dropwise with stirring. The reaction mixture was left overnight for evaporation of the ammonia, the residue was decomposed by stirring with 100 ml of water, the organic layer was separated, the aqueous layer was extracted with ether, and the combined extract was washed with 5% hydrochloric acid and dried with magnesium sulfate; the alcohol and ether were then distilled off. The residual crystals melted at 96-97°. Yield 14.5 g (71.7%). A mixture of these crystals with trans-tetramethylbutenediol prepared from dimethyl fumarate (m. p. 95-96°) melted without depression.

No additional quantity of the glycol could be isolated after percolation of the aqueous solution with ether for 10 hours.

Hydrogenation of tetramethylbutynediol. 17.6 g of tetramethylbutynediol in 250 ml of absolute ether was hydrogenated in presence of 0.17 g of 10% Pd/$CaCO_3$ [34] until 2.864 liters of hydrogen (18°, 743 mm) had been absorbed. After filtration followed by distillation of the ether, a crystalline product (16.4 g) was obtained with m. p. 62.5-69°. 16.4 g of the hydrogenated mixture was dissolved by heating in 200 ml of ligroine (b. p. 50-60°). Crystals with m. p. 66-70° were deposited on cooling. Three recrystallizations of these crystals from ligroine (b. p. 50-60°) led to deposition of 6.35 g of crystals with m. p. 74-75.5°.

The solvent was partly distilled off from the mother liquor. The resulting crystals melted at 63-69° after recrystallization from ligroine. Two recrystallizations of this fraction gave 3 g of crystals with m. p. 68-69°. The residual mixture of crystals (5.9 g) was fractionated in the following manner. A few portions of dilute solutions of these crystals in ligroine (b. p. 50-60°) were made up (1 g of substance in 100 ml of ligroine). After partial evaporation of the solvent at room temperature, crystals in the form of short rods (m. p. 68-69°) were separated mechanically. The residue was redissolved in ligroine. Four repetitions of this procedure followed by mechanical selection yielded 1.85 g of cis-isomer (m. p. 69°), 0.5 g of substance with m. p. 75°, and 0.17 g of trans-form (m. p. 96-97°). A mixed sample of crystals with m. p. 96-97° and trans-tetramethylbutenediol did not give a depression.

The remaining crystals were sorted into two portions – one enriched with molecular compound (1.5 g) and one enriched with cis-form (0.8 g).

The first portion was chromatographed on 25 g of alumina. Elution with ligroine (b. p. 50-60°) gave 0.45 g of cis-tetramethylbutenediol (m. p. 68-69°) and elution with benzene gave a further 0.2 g of the same product (m. p. 68-69°). Elution with a mixture of methanol and ether (1:1) gave 0.35 g of trans-tetramethylbutenediol (m. p. 95-96°). 0.1 g of substance with m. p. 74-75° was eluted with methanol.

The second portion was chromatographed on 15 g of alumina. 0.6 g of cis-tetramethylbutenediol (m. p. 68-69°) was eluted with ligroine (b. p. 50-60°), and a small quantity of trans-tetramethylbutenediol (m. p. 95-96°) with a mixture of methanol and ether (1:1). A very small quantity of substance with m. p. 75° was eluted with methanol.

Determination of the composition of a mixture of tetramethylbutenediols by the spectral method. Measurement of the spectrum of the hydrogenated mixture was carried out at two points in the 1600 cm^{-1} region and at two points in the 1400 cm^{-1} region. The following values of absorption coefficients (χ) were obtained: χ_{1662} 1.00, χ_{1634} 0.93, χ_{1453} 3.12, χ_{1457} 3.12. The relative amounts of cis- and trans-isomers were calculated from the ratios of the respective absorption coefficients with the help of the calibration graph (Fig. 4):

$$\frac{\chi_{1662}}{\chi_{1634}} = 1.07;\ \%\ \text{trans} - 16;\ \%\ \text{cis} - 84;$$

$$\frac{\chi_{1453}}{\chi_{1457}} = 1.00;\ \%\ \text{trans} - 12;\ \%\ \text{cis} - 88.$$

The relative error of the method was estimated with the help of a specially prepared mixture containing 92.02% of cis-tetramethylbutenediol and 7.98% of trans-isomer. The following values of absorption coefficients were obtained: χ_{1662} 0.68, χ_{1634} 0.61, χ_{1453} 3.36, χ_{1451} 4.02:

$$\frac{\chi_{1662}}{\chi_{1634}} = 0.83;\ \%\ \text{trans} - 6;$$

$$\frac{\chi_{1453}}{\chi_{1451}} = 1.12;\ \%\ \text{trans} - 5.$$

The mean content of trans-isomer is 5.7%. The relative experimental error is 30%.

Preparation of the molecular compound with m. p. 74°. 0.75 g of cis-tetramethylbutenediol (m. p. 69-70°) and 0.25 g of trans-tetramethylbutenediol (m. p. 95-96°) was dissolved in absolute ether. After the ether had been driven off, the residue (1 g) had m. p. 73-74°. After recrystallization from ligroine, the crystals melted at 73.5-74° A mixture of these crystals with the substance with m. p. 74.5° obtained by hydrogenation of tetramethylbutynediol melted at 73-73.5°.

Investigation of the molecular compound with m. p. 74°. Two layers formed when the substance with m. p. 74-74.5° was heated with water. The layers were separated. Cooling of the upper layer caused crystals with m. p. 68-69° to come down (no change in melting point after recrystallization from ligroine). Evaporation of the aqueous solution in vacuo led to deposition of crystals with m. p. 73-73.5°; after recrystallization from ligroine (b. p. 35-50°), the m. p. was 74.5°. The mother liquor yielded a small quantity of crystals with m. p. 92-93° (after 3 recrystallizations from toluene). A mixed test of the crystals with m. p. 92-93° and transtetramethylbutenediol with m. p. 95-96° (obtained from dimethyl fumarate) melted at 92.5-94°.

1 g of the substance with m. p. 74-75.5° was dissolved in ligroine (b. p. 50-60°) and chromatographed on 20 g of alumina. Elution with ligroine removed 0.45 g of cis-tetramethylbutenediol (m. p. 68-69°); elution with benzene removed 0.2 g of rather less pure substance with m. p. 67-69°. Elution with 1:1 methanol/ether and with pure methanol yielded 0.35 g of substance with m. p. 72-75°. Estimation of the composition of the molecular complex with the help of the calibration diagram (Fig. 4) gave the following values: χ_{1662} 0.62, χ_{1634} 0.55, χ_{1453} 6.94, χ_{1457} 6.22:

$$\frac{\chi_{1662}}{\chi_{1634}} = 1.13;\ \%\ \text{trans} - 27;$$

$$\frac{\chi_{1453}}{\chi_{1457}} = 1.11;\ \%\ \text{trans} - 24.$$

Preparation of the molecular complex with m. p. 101°. 0.2 g of trans-tetramethylbutenediol (m. p. 95-96°) and 0.2 g of tetramethylbutynediol (m. p. 93-94°) were dissolved in 25 ml of absolute ether. After the ether had been distilled off, the residue (0.4 g) melted at 100-101.5°. After recrystallization from ligroine (b. p. 50-60°), the crystals had m. p. 100.5-101.5°.

The composition of the complex was estimated by the spectral method on the basis of comparison of the intensities of absorption of the complex at 1662 and 1453 cm^{-1} with the corresponding intensities of pure trans-tetramethylbutenediol and tetramethylbutynediol. Measurement of the spectra gave the following values of absorption coefficients:

	χ_{1662}	χ_{1453}
Trans-tetramethylbutenediol	0.75	3.48
Tetramethylbutynediol	0.50	1.78
Complex	0.55	2.26

On the basis of the Lambert-Beer law it was then calculated that the complex is made up of 38% of tetramethylbutenediol and 62% of tetramethylbutynediol.

Attempts to isomerize cis-tetramethylbutenediol. 2.5 g of cis-tetramethylbutytnediol (m. p. 69-70°) was dissolved in 60 ml of ligroine (b. p. 50-60°) and shaken for 40 hours in a hydrogen atmosphere over poisoned Lindlar catalyst [32].

Crystals with m. p. 68-70° (2.5 g) were isolated after filtration and distillation of the solvent.

Hydrogenation of tetramethylbutynediol over poisoned catalyst. To a mixture of 0.5 g of 10% Pd/$CaCO_3$, 6 ml of anhydrous methanol and 2 drops of quinoline saturated with hydrogen was added 0.5 g of tetramethylbutynediol in 6 ml of anhydrous methanol. Hydrogenation (21°, 746 mm) led to absorption of 75 ml (approx. 1 mole) of hydrogen, after which there was marked slowing down of hydrogenation. The methanol was distilled off and the residual crystals (m. p. 60-65°) were recrystallized from ligroine. Two fractions were collected: m. p. 63-66° (0.3 g) and m. p. 80-82.5° (0.14 g).

Spectral analysis of the unresolved product of hydrogenation (using the calibration graph in Fig. 4) established that it contained 6-8% of trans-tetramethylbutenediol.

Preparation of trans-2-butene-1,4-diol. This compound was synthesized by Valette's method [25]. 120 g of trans-1,4-dibromo-2-butene gave 82 g (80%) of trans-2-butene-1,4-diol diacetate (b. p. 113° (11 mm), $n^{20}D$ 1.4422, m. p. 13-14.5°), which on saponification gave the trans-diol in 79% yield (b. p. 135° (13 mm), $n^{20}D$ 1.4770, m. p. 25°). Trans-2-butene-1,4-diol dibenzoate melted at 98.5-100° (from alcohol). The literature gives m. p. 99-100° [30].

Hydrogenation of butynediol. A solution of 30 g of freshly distilled butynediol in 350 ml of absolute methanol was hydrogenated in presence of 3 g of 10% Pd/$CaCO_3$ until 8475 ml of hydrogen (19°, 760 mm, 9 hours) had been taken up. After filtration and distillation of the methanol, the product was distilled in vacuo. 3 fractions were collected: 1st, 60-120° (13 mm), 3 g; 2nd, 135-136° (13 mm) $n^{19}D$ 1.4680, 19.3 g; 3rd, 136-141° (13 mm), $n^{19}D$ 1.4678, 4 g; residue 3.6 g.

The dibenzoate of cis-2-butene-1,4-diol was obtained from the 2nd fraction; m. p. 69-70° (from alcohol); the literature reports m. p. 65-66° [30].

The composition of the mixture of butenediols was determined on the basis of the Lambert-Beer law by comparison of the intensities of the absorption bands of the mixture and of pure trans-isomer in the 1600 and 900 cm^{-1} regions (see Figs. 2 and 3). The following absorption coefficients (in dioxane) were found: for pure trans-butenediol χ_{1677} 0.31; χ_{976} 5.04; for the hydrogenated mixture χ_{1677} 0.06; χ_{976} 0.86. Hence values of 19 and 17% were obtained respectively for the content of trans-isomer in the hydrogenated mixture.

Hydrogenation of butynediol diacetate. 44 g of butynediol diacetate (b. p. 106° at 13 mm, m. p. 29°) was hydrogenated in 65 ml of methanol in presence of 1.3 g of 10% Pd/$CaCO_3$; 1 mole of hydrogen (5.79 liters at 22°, 740 mm) was absorbed in 1 hour 15 minutes. After filtration and fractionation, 32 g of a mixture of cis- and trans-butenediols was obtained; b. p. 113-118° (12 mm), $n^{20}D$ 1.4422; residue 8 g.

The composition of the hydrogenated mixture was determined, after the same fashion as that of the mixture of butenediols, by comparison of the intensity of the absorption band at 1626 cm^{-1} (in dioxane); values of χ_{1626} 0.73 and χ_{1626} 0.25 were obtained for pure trans-butenediol acetate and the hydrogenated mixture respectively; hence the content of trans-isomer in the hydrogenated mixture was 34%. The relative error was found to be ±16% by measurements on a mixture enriched with a known quantity of the trans-form.

Reduction of dimethyl fumarate and maleate with lithium aluminum hydride. To an ethereal solution of 6.9 g of $LiAlH_4$ was added, with stirring, a solution of 8 g of dimethyl fumarate in 200 ml of absolute ether at such a rate that the ether was gently boiling (8-9 hours). Stirring was continued for 4 days at room temperature. The resulting complex was decomposed with 20% sulfuric acid. The ether layer was collected and the aqueous layer was thoroughly extracted with ether. The combined ethereal solution was dried with potassium carbonate. After the ether had been removed, a fraction with b. p. 102-104° (2 mm), $n^{19}D$ 1.4612 (2.4 g) was collected; the resinous residue weighed 0.8 g. The aqueous solution was saturated with potassium carbonate until neutral, and then percolated with ethyl acetate (50 hours). 1 g of a substance with $n^{20}D$ 1.4709 was isolated. A dibenzoate with m. p. 80.5-81.5° (from alcohol) was prepared from the fraction with b. p. 102-104° (2 mm).

Found %: C 72.17, 72.08; H 6.02, 6.14. $C_{18}H_{18}O_4$. Calculated %: C 72.49; H 6.07.

Under the same conditions 8 g of dimethyl maleate gave 0.75 g of a fraction with b. p. 130-136° (13 mm), $n^{20}D$ 1.4628, and 2.6 g of undistillable residue. The fraction with b. p. 130-138° (13 mm) gave a dibenzoate with m. p. 80.5-81.5° (from alcohol).

A mixture of the dibenzoates of the glycols obtained by reduction of fumaric and maleic esters melted without depression. The mixture of these dibenzoates with the dibenzoate of the butanediol (m. p. 81-82°) obtained by hydrogenation of butynediol likewise melted without depression.

SUMMARY

1. Hydrogenation of butynediol and 2,5-dimethyl-3-hexane-2,5-diol (tetramethylbutynediol) over $Pd/CaCO_3$ converts them into mixtures of stereoisomeric olefinic glycols containing from 10 to 20% of trans-form. Hydrogenation of butynediol diacetate leads to 30 to 40% of trans-form.

2. The trans-forms are not produced by isomerization of the cis-olefinic compounds but probably with participation of free radicals during the hydrogenation; this theory is supported by the considerable polymerization that is observed during the hydrogenation of butynediol and its acetate.

3. Cis- and trans-tetramethylbutenediols form a stable crystalline complex in which the isomeric glycols are linked by a hydrogen bond. The complex is substantially undissociated in nonpolar solvents. A similar complex is formed by trans-tetramethylbutenediol with tetramethylbutynediol.

4. Tetramethylbutynediol is hydrogenated over Pd catalyst more quickly than tetramethylbutenediol, whereas butynediol absorbs hydrogen more slowly than butenediol.

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INVESTIGATION OF THE VAPOR-PHASE CATALYTIC HYDRATION OF ACETYLENE AND ITS DERIVATIVES

II. HYDRATION OF ETHYNYLBENZENE, TERT. BUTYLACETYLENE, DIMETHYLACETYLENE, METHYLETHYLACETYLENE AND ETHYLVINYLACETYLENE

Iu. A. Gorin and L. P. Bogdanova

Hydration of mono- and disubstituted acetylenes leads to formation of ketones. These reactions (like the reaction with acetylene) are realized in the liquid phase in presence of mercury salts. Mowat and Smith [1] added water to 2-pentyne in presence of mercuric sulfate and obtained a mixture of diethyl and methyl propyl ketones. Hennion and others [2] hydrated 1-hexyne, 1-octyne, 1-heptyne and dibutylacetylene in aqueous solutions of methanol or acetone in presence of $HgSO_4$. The reaction products were the corresponding ketones. I. N. Nazarov [3] performed the hydration of hydrocarbons of the divinylacetylenic series. Sherrill and Smith [4] hydrated 9,10-undecynoic acid and obtained a mixture of two ketoacids. E. D. Venus-Danilova and S. N. Danilov [5] hydrated primary acetylenic alcohols.

Hydration of acetylenic derivatives in aqueous solutions in presence of mercuric sulfate usually proceeds satisfactorily if the acetylenic compound or the product of its hydration is soluble in water. The method does not usually give good results if the compounds are insoluble in water.

In our preceding communication [6] we presented the results obtained for hydration of vinylacetylene on solid catalysts not containing mercury compounds. In the present work we investigated the possibility of hydration of other mono- and disubstituted derivatives of acetylene over cadmium-calcium phosphate catalyst. We showed that this simple method is a route from acetylenic derivatives to ketones of various structures. Vapor-phase hydration proceeds extremely effectively with monosubstituted acetylenic derivatives. The process proceeds less intensively with disubstituted derivatives, presumably due to the special features of their structure which results in reaction at lower velocities and with lower yields of hydration products – ketones.

Pyrolysis of methane to acetylene is accompanied by formation of small quantities of substituted acetylenes. In connection with the projected industrial realization of such processes (for acetylene manufacture) in our country, the possibility may arise of certain acetylene derivatives becoming accessible products which might serve as starting substances for ketones.

Our investigations of the hydration of various acetylenic hydrocarbons over cadmium-calcium phosphate catalyst enable us to arrange them in order of activity (expressed as degree of transformation of the hydrocarbons under uniform experimental conditions: space velocity 100 l/l cat. hr., temperature 375°, and hydrocarbon/water ratio 1:10). These data are presented in Table 1.

The table indicates that the degree of transformation of a monosubstituted acetylenic hydrocarbon depends on the nature of the radical at the acetylenic bond. Acetylene is intermediate between ethynylbenzene and tert.-butylacetylene in respect of activity during hydration in the vapor phase. Substituting groups may be arranged in the following order in respect of their effect on the triple bond:

$$C_6H_5- \rangle (CH_3)_3C- \rangle CH_2=CH-.$$

The degree of transformation of disubstituted derivatives is nearly one-half of that of monosubstituted derivatives.

TABLE 1

Comparison of Activity of Hydrocarbons of the Acetylenic Series During Vapor-Phase Hydration over Cadmium-Calcium Phosphate Catalyst

Name		Degree of transformation of hydrocarbon %	Yield of carbonyl compounds, as mole-% of reacted hydrocarbon
of acetylenic hydrocarbon	of carbonyl compound obtained		
Ethynylbenzene	Acetophenone	76.0	64.0
Acetylene	Acetaldehyde	71.0	67.0
Tert.-butylacetylene	Pinacoline (3,3-dimethyl-2-butanone)	64.0	75.0
Vinylacetylene	Methyl vinyl ketone	36.5	70.5
Dimethylacetylene	Methyl ethyl ketone	38.5	37.2
Methylethylacetylene	Mixture of methyl propyl ketone and diethyl ketone	34.3	35.0
Ethylvinylacetylene	Ethyl propenyl ketone	21.8	40.4

On the basis of the previously enunciated ideas [7, 8] about the nature of the interaction of acetylene with the copper ion, we put forward a mechanism of the hydration of acetylene and acetylenic hydrocarbons over solid, ionic catalysts that accounts broadly for the activation of the acetylenic molecule and its action on water. This mechanism is based on the concept of interaction of the acetylenic molecule with elements of the lattice, leading to polarization of the acetylene and to formation of a complex. According to the literature [9], and in the light of the results of Iu. A. Gorin and I. K. Gorn [10], various salts and oxides of cadmium, copper and zinc are catalysts for the hydration of acetylene. We therefore assume that cations of these metals serve as the activating agent in the present case.

We shall now consider the hydration of acetylene in presence of cadmium-calcium phosphate catalyst. We designate by Cd^+ the cation of the cadmium phosphate lattice* that acts on acetylene (making the assumption that it has a definite positive charge whose magnitude depends on the degree of ionization of the atoms and atomic groups in the crystal lattice [11]). Adsorption of a molecule of acetylene on the surface of the catalyst causes it to fall into the sphere of action of a cadmium ion so that it becomes polarized, the π-electron of the triple bond being shifted toward the positively charged cation of the lattice (Cd^+). This interaction of polarized acetylene molecules and Cd^+ leads to formation of a complex with a positive charge at one of the carbon atoms:

$$CH\equiv CH + Cd^+ \longrightarrow \overset{\delta+}{C}H\equiv \overset{\delta-}{C}H + Cd^+ \longrightarrow \overset{\delta+}{C}H=CH \dashrightarrow Cd$$

The broken arrow designates a bond in the complex formed at the expense of transfer of electrons from a polarized acetylenic molecule to a positively charged cadmium ion. A molecule of water is also adsorbed by the surface of the catalyst and its degree of polarization increases under the influence of lattice ions. A polarized molecule of water reacts with the polar complex, forming vinyl alcohol which further isomerizes to acetaldehyde. During this stage the lattice cation is regenerated**.

$$Cd \dashleftarrow CH=\overset{\delta+}{C}H + HOH \longrightarrow Cd^+ + CH_2=CHOH \longrightarrow CH_3CHO$$

* According to [12] calcium phosphate does not catalyze the hydration of acetylene, and it only functions as a carrier in presence of copper and cadmium phosphates.

** The results of the present work, including the mechanism of hydration of acetylene and its derivatives over cadmium-calcium phosphate catalyst, were submitted on December 3, 1956 to the Scientific Council of the All-Union Scientific Research Institute for Synthetic Rubber (see protocol no. 19). On January 11, 1957 the All-Union Institute received a manuscript from E. N. Tsybina, A. I. Gel'bshtein and M. I. Temkin in which the authors submit a mechanism basically similar to ours for the hydration of acetylene over a zinc phosphate catalyst.

The hydration of acetylenic derivatives over solid catalysts proceeds according to a mechanism that should not differ from the mechanism of hydration of acetylene. In the present case, however, unsymmetrical molecules of acetylenic derivatives must differ from acetylene in possessing a certain polarity due to the influence of substituents. This influence accounts for the presence of a dipole moment in compounds of the type in question [13]. The distribution of the electronic density may be represented by the following scheme for monosubstituted acetylenic hydrocarbons:

$$(CH_3)_3C-\overset{\delta^+}{C}\equiv\overset{\delta^-}{C} + Cd^+ \longrightarrow (CH_3)_3C-\overset{\delta^+}{C}=CH \dashrightarrow Cd$$

In the reaction of a water molecule with the polar complex, the negatively charged hydroxyl group adds on to the positively charged carbon atom:

$$(CH_3)_3C-\overset{\delta+}{C}=CH \dashrightarrow Cd + HOH \longrightarrow Cd^+ + (CH_3)_3C-COH=CH_2 \rightarrow$$
$$\rightarrow (CH_3)_3C-CO-CH_3$$

It follows from the data of Table 1 that acetylene and its derivatives (ethynylbenzene and tert.-butylacetylene) differ from one another in degree of transformation, but this difference is relatively small. The substituent at the triple bond probably creates a steric hindrance to the hydration of monosubstituted acetylenic hydrocarbons; the inhibiting effect of the steric factor may, however, be offset by the influence of the substituent and by the degree of polarity and polarizability of the acetylenic hydrocarbon. For this reason the rates of hydration of monosubstituted derivatives generally do not differ greatly from the rate of hydration of acetylene. The considerable difference in the degree of transformation during hydration of vinylacetylene may be explained by the effect of conjugation of the double and triple bonds which equalizes the electronic density and lowers the degree of polarization of the acetylenic bond.

The rate of transformation of disubstituted acetylenic hydrocarbons is approximately half that of the rate of transformation of monosubstituted acetylenes. It is highly probable that steric hindrance is responsible for this inhibition in presence of two substituent groups.

Two substituents at the triple bond may influence not only the reaction rate (which determines the degree of transformation) but also the structure and composition of the products obtained. A hydroxyl group may join on at the triple bond of a disubstituted acetylenic hydrocarbon at either the α or the β carbon atom:

$$R-\underset{\alpha}{C}\equiv\underset{\beta}{C}-R_1$$

If R and R_1 are the same, a single product is obtained by hydration. If they are different, the direction of the reaction will evidently be governed by the competing influence of the substituents. The amounts of isomers formed will be approximately equal when there is little difference in the actions of the two groups. Hydration of methylethylacetylene, for example, leads to two isomers – diethyl ketone and methyl propyl ketone. But if the radicals are very unequal in activity, then only one product will be formed. An example is ethylvinylacetylene, hydration of which gives only ethyl propenyl ketone. We assume that the enol form is an intermediate in this reaction and subsequently isomerizes to ethyl propenyl ketone:

$$CH_3-CH_2-\overset{\delta^+}{C}\equiv\overset{\delta^-}{C}-CH=CH_2 + Cd^+ \longrightarrow CH_3-CH_2-\overset{\delta^+}{C}=C(CH=CH_2) \dashrightarrow Cd + HOH \longrightarrow$$
$$\longrightarrow Cd^+ + CH_3-CH_2-C(OH)=CH-CH=CH_2 \longrightarrow CH_3-CH_2-CO-CH=CH-CH_3$$

An alternative explanation of the formation of ethyl propenyl ketone involves a considerable shift of the electron density along the conjugated chain towards the enol group (due to the polarizing effect of the ethyl radical [14]), the addition of the elements of water in the 1-4 position, and isomerization of the intermediately formed allenic enol form:

$$CH_3-CH_2-\overset{\delta^+}{C}\equiv C-CH=\overset{\delta^-}{C}H_2 + Cd^+ \longrightarrow CH_3-CH_2-\overset{\delta^+}{C}=C=CH-CH_2 \dashrightarrow Cd + HOH \longrightarrow$$
$$\longrightarrow Cd^+ + CH_3CH_2C(OH)=C=CH-CH_3 \longrightarrow CH_3-CH_2COCH=CH-CH_3 .$$

No absolute proof has of course been obtained as yet of our proposed mechanisms. It is necessary to carry out further investigations of the behavior of other representatives of the acetylenic hydrocarbon series during hydration in the vapor phase. It should then be possible to obtain ample data to establish the validity or otherwise of the concepts here put forward.

EXPERIMENTAL

Substances, Apparatus, and Experimental Procedure

Dimethylacetylene was prepared by cleavage (with alcoholic alkali) of hydrogen chloride from 2,2-dichlorobutane; the latter was obtained by chlorination of methyl ethyl ketone with PCl_5 by the procedure of A. E. Favorskii [15]. B. p. 27-27.2°, d^{20}_4 0.7128, $n^{25}D$ 1.3891.

Ethynylbenzene* with b. p. 142-143°, d^{12}_4 0.9368, $n^{17}D$ 1.5503.

Tert.-butylacetylene was prepared by removing hydrogen chloride (with alcoholic alkali) from 2,2-dichloro--3-methylbutane. B. p. 39.5°, d^{15}_4 0.6732, $n^{15}D$ 1.3772.

Methylethylacetylene was prepared by removing hydrogen chloride from 3,3-dichloropentane. B. p. 56-56.5°, d^{17}_4 0.7121, $n^{23}D$ 1.4042.

Ethylvinylacetylene** was prepared by the method of Carothers [16]. B. p. 83.5-84.0°, d^{20}_4 0.7479, $n^{20}D$ 1.4522.

Acetylene was obtained from a cylinder. It was purified by passage through sodium hypochlorite solution before entering the converter.

Vinylacetylene. The commercial product was used (obtained by dimerization of acetylene).

Catalyst. A mixture of cadmium and calcium phosphates was prepared from a mixture of cadmium nitrate and calcium acetate solutions by precipitation with ammonium phosphate [17]. The precipitate was washed and dried at 110°. Tablets were prepared from the powder in a laboratory hydraulic press.

Hydration of the liquid hydrocarbons was undertaken in a quartz tube filled with the catalyst (10 ml) and placed in an electric furnace. The reaction temperature was measured with a thermocouple. Liquid hydrocarbon and water were proportioned from burets; the buret containing the hydrocarbon was cooled with ice. The reaction products were passed through a condenser and collected in a receiver which was also cooled with ice or a mixture of ice and salt (depending upon the boiling point of the original hydrocarbon). Each experiment extended over 1.5 hours. After an experiment the catalyst was regenerated in a mixture of air and steam at 450°.

Hydration of Hydrocarbons

Hydration of ethynylbenzene. The liquid products consisted of two layers – aqueous and oily. The layers were separated, and the quantity of carbonyl compounds was determined in the aqueous layer by reaction with hydroxylamine hydrochloride. The oily layer was fractionally distilled to give two fractions: 1st with b. p. 49-50° (14 mm), $n^{17}D$ 1.5500 (unreacted ethynylbenzene); 2nd, b. p. 83-85° (12 mm), acetophenone; d^{25}_4 1.0229, $n^{20}D$ 1.5339.

Found %: C 80.9; H 7.2. M 116.5, 118.5. C_8H_8O. Calculated %: C 80.00; H 6.67. M 120.

Acetophenone semicarbazone with m. p. 196-197° was prepared.

Literature data [18] for acetophenone: b. p. 83-85° (12 mm), d^{25}_4 1.0236, $n^{20}D$ 1.5342; semicarbazone m. p. 195-198°.

Hydration of tert.-butylacetylene. Fractional distillation of the condensate gave two fractions: 1st, b. p. 39.5°, $n^{15}D$ 1.3770 (unreacted tert.-butylacetylene); 2nd, an azeotrope of 3,3-dimethyl-2-butanone with water, boiling at 85°. The azeotrope was dried with calcium chloride and redistilled to give 3,3-dimethyl-2-butanone

* Obtained from T. A. Favorskaia.

** Obtained from A. A. Petrov.

with b. p. 102-104°, d^{20}_4 0.8017.

Found %: C 72.21; H 12.43. M 97.5. $C_6H_{12}O$. Calculated %: C 72.0; H 12.0. M 100.

3,3-Dimethyl-2-butanone oxime with m. p. 74.5-75° was prepared.

Literature data [19a] for 3,3-dimethyl-2-butanone: b. p. 102-104°, d^{20}_4 0.7999; oxime, m. p. 74.5-75°.

Hydration of dimethylacetylene. Fractional distillation of the reaction products gave: 1st b. p. 27-27.2° (unreacted dimethylacetylene); 2nd, b. p. 72-73° – azeotrope of methyl ethyl ketone with water. The azeotrope was dried with calcium chloride and the product was again fractionally distilled to give methyl ethyl ketone.

B. p. 80°, d^{20}_4 0.8051, $n^{20}D$ 1.3782. M 71.5, 72.0. C_4H_8O. Calculated: M 72.0.

The semicarbazone of methyl ethyl ketone with m. p. 139-140° was prepared.

Found %: 46.55, 46.26; H 8.81, 8.82. $C_5H_{11}ON_3$. Calculated %: C 46.51; H 8.52.

Literature data [19b] for methyl ethyl ketone: b. p. 80°, d^{20}_4 0.8058, $n^{20}D$ 1.3788; semicarbazone with m. p. 140°.

Hydration of methylethylacetylene. Fractional distillation of the liquid products gave the following fractions: 1st, b. p. 56-56.5°, $n^{20}D$ 1.4041 (unreacted methylethylacetylene); 2nd, b. p. 82-82.9°, azeotrope of the ketones formed in the reaction and water. After drying with calcium chloride, the product was redistilled and a fraction with b. p. 101.5-102°, d^{20}_4 0.8106, $n^{20}D$ 1.3901 was isolated.

Found %: C 70.53, 69.93; H 11.83, 11.32. M 82.8, 83.1. $C_6H_{10}O$. Calculated %: C 69.76; H 11.63. M 86.

The semicarbazone of the ketones was prepared; after numerous recrystallizations from alcohol it melted at 83°.

Literature data [19, c,d] for diethyl ketone: b. p. 101.5-102°, d^{20}_4 0.8159, $n^{20}D$ 1.3922; semicarbazone with m. p. 139°. For methyl propyl ketone: b. p. 102°, d^{20}_4 0.8089, $n^{20}D$ 1.3894; semicarbazone m. p. 110°.

The product of hydration of methylethylacetylene is evidently a mixture of two isomeric ketones. The elementary composition of the mixture and its molecular weight correspond to each of the isomers. The densities and refractions of the mixture are intermediate between the values for each of the isomers. The melting point of the mixture of the semicarbazones of the ketones is lower than the melting point of either substance separately.

Hydration of ethylvinylacetylene. The carbonyl compounds were extracted from the condensate with ligroine. A ketone was isolated on distillation of the ethereal extract.

B. p. 35-36° (10 mm), d^{20}_4 1.8543, $n^{20}D$ 1.4384; semicarbazone m. p. 157-160°.

Due to the speed of polymerization of the ketone and its small quantity, it was impossible to determine its boiling point at atmospheric pressure. Comparison with the literature data indicates that the product is ethyl propenyl ketone. A scheme for its formation was given previously.

Literature data [19e] for ethyl propenyl ketone: b. p. 140-140.6°, d^{20}_4 0.8558, $n^{20}D$ 1.4391; semicarbazone m. p. 160°.

Hydration of acetylene and vinylacetylene was effected by the procedure described in the preceding communication [6]. Acetaldehyde in the product of hydration of acetylene, and methyl vinyl ketone in the product of hydration of vinylacetylene were determined with the help of hydroxylamine hydrochloride. The proportion of unreacted hydrocarbons was determined from the content of unsaturated compounds in the exit gas.

Mean values from three to four parallel experiments (degree of transformation of the acetylenic hydrocarbon and yield of carbonyl compounds) are presented in Table 1.

We extend our profound thanks to T. A. Favorskaia and A. A. Petrov for provision of ethynylbenzene and ethylvinylacetylene.

SUMMARY

1. A study was made of the hydration of some mono- and disubstituted acetylene homologs over cadmium-calcium phosphate catalyst in the vapor phase.

2. The degrees of transformation of some monosubstituted acetylenes during vapor-phase hydration over solid catalyst under identical experimental conditions were compared. It was established that their activity depends on the nature of the radical at the triple bond.

3. Under the same conditions disubstituted acetylenes are hydrated more slowly than monosubstituted derivatives.

4. Schemes are proposed for the process of hydration of acetylene and its derivatives over solid catalysts in the vapor phase.

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THE MECHANISM OF THE CATALYTIC ACTION OF ALUMINUM CHLORIDE

VI. MORE ABOUT THE KINETICS AND MECHANISM OF THE ALKYLATION OF BENZENE WITH CHLORO DERIVATIVES

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After one of our previous communications [1] had been printed, we had the opportunity of seeing the paper by Brown and Grayson [2] on the kinetics of alkylation of benzene with some halogenated compounds in the same solvent – nitrobenzene. They confirmed that the reaction was monomolecular with respect to the halogen compound and the aromatic compound, but their results were markedly different from ours for the order of reaction with respect to aluminum chloride and concerning the influence of the solvent. In the above authors' experiments, replacement of 60% of the nitrobenzene by methylcyclohexanone or benzene did not have a serious effect on the reaction rate, which was proportional to the concentration of aluminum chloride. We decided to make a more extensive investigation of this reaction in view of the necessity for explaining the wide discrepancy between the results of Brown and Grayson and our own, and also in view of the great importance of these results for generalization of the mechanism of the reaction.

Starting substances and experimental technique. The chloro compounds used in this work were cyclohexyl chloride (b. p. 142.5-143°, $n^{20}D$ 1.4612), tert. butyl chloride (b. p. 51.5-52°, $n^{20}D$ 1.3900), and tert. amyl chloride (b. p. 85-86°, $n^{20}D$ 1.4059). They were prepared from the corresponding alcohols and hydrochloric acid; the products were twice distilled through a column, and the middle cuts were collected. Employment of nitrobenzene as solvent for aluminum chloride and homogenization of the reaction mass enabled us to use solvents (apart from benzene, nitrobenzene and carbon disulfide) in the shape of rather less active chloro derivatives that do not react with benzene under these conditions (1,2-dichloroethane, 1,1,2,2-tetrachloroethane and carbon tetrachloride). The latter were purified with concentrated sulfuric acid and distilled from a column; middle cuts boiling in a range of 0.5-1° were collected. The carbon disulfide was purified with mercury. Purification methods and the quality of the benzene were the same as before [1].

The reaction mass was prepared from appropriate volumes of nitrobenzene, 10% aluminum chloride solution in nitrobenzene, solvent and benzene. The quantity of alkyl chloride taken was always such that its starting concentration was 0.200 mole/liter. In order to avoid polyalkylations, the benzene was always used in 7-8-fold excess in relation to the halogen compound. The previously described procedure [1] for estimation of the quantity of hydrogen chloride formed was applied in order to follow the course of the reactions. The data for solubility of hydrogen chloride in carbon tetrachloride, carbon disulfide, and dichloro- and tetrachloroethane, required for these observations, were determined by holding the solutions in a thermostat for 4 hours at the required temperature and by subsequent titration of the hydrogen halide present in the liquid and gas phases. (These data had previously been obtained for benzene and nitrobenzene [1].) Results are presented in Table 1. The values for carbon tetrachloride, dichloroethane and tetrachloroethane are 10-20% lower than those reported by Bell [3], probably because we used fairly anhydrous substances.

Reaction order with respect to aluminum chloride. With the objective of confirming our earlier data for a mixed solvent comprising benzene and nitrobenzene [1], we carried out a similar investigation for a mixture of nitrobenzene and carbon tetrachloride, using tert. butyl and amyl chlorides as alkylating agents (Tables 2 and 3). Experiments were run at 20 ± 0.05° and with a benzene concentration of 12.5 vol.-%.

TABLE 1

Number	Solvent and temperature	Concentration of HCl (moles)		Solubility α	
		solution	gas phase		
1	1,2-Dichloroethane, 20°	0.169	0.0142	11.90	11.85
2		0.218	0.0187	11.67	
3		0.097	0.0081	11.97	
4	1,2-Dichloroethane, 40°	0.078	0.0101	7.72	7.8
5		0.136	0.0174	7.82	
6	Carbon tetrachloride, 20°	0.0294	0.0078	3.77	3.85
7		0.0923	0.0233	3.96	
8		0.0544	0.0142	3.83	
9	Carbon tetrachloride, 10°	0.0393	0.0095	4.14	4.15
10		0.0624	0.0150	4.17	
11	1,1,2,2-Tetrachloroethane, 20°	0.0772	0.0140	5.51	5.5
12		0.0489	0.0089	5.49	
13	1,1,2,2-Tetrachloroethane, 10°	0.110	0.0179	6.14	6.0
14		0.076	0.0130	5.84	
15	Carbon disulfide, 20°	0.0442	0.0076	5.82	5.85
16		0.0674	0.0115	5.87	
17	Carbon disulfide, 10°	0.135	0.0164	8.23	8.1
18		0.097	0.0122	7.95	

TABLE 2

Reaction of Tert. Butyl Chloride with Benzene

Concentration of aluminum chloride (moles)	Composition of medium (vol-%)		Number of parallel experiments	Velocity constant κ_1 (min $^{-1}$)	Order of reaction with respect to $AlCl_3$
	CCl_4	nitrobenzene			
0.203	60.3	25.0	5	0.055 ± 1.4%	1.68
0.100	60.3	25.0	3	0.0167 ± 1.55%	
0.203	48.0	37.5	4	0.146 ± 2.3%	1.33
0.100	48.0	37.5	4	0.057 ± 0.6%	
0.100	35.5	50.0	3	0.202 ± 2.05%	1.12
0.049	35.5	50.0	4	0.091 ± 1.4%	

TABLE 3

Reaction of Tert. Amyl Chloride with Benzene

Concentration of aluminum chloride (moles)	Composition of medium (vol-%)		Number of parallel experiments	Velocity constant κ_1 (min $^{-1}$)	Order of reaction with respect to $AlCl_3$
	CCl_4	nitrobenzene			
0.203	35.5	50.0	4	0.121 ± 2.5%	0.93
0.100	35.5	50.0	3	0.063 ± 1.4%	
0.100	23.0	62.5	5	0.179 ± 3.0%	0.85
0.049	23.0	62.5	4	0.098 ± 1.4%	
0.049	10.5	75.0	4	0.255 ± 3.7%	0.77
0.025	10.5	75.0	4	0.147 ± 1.25%	

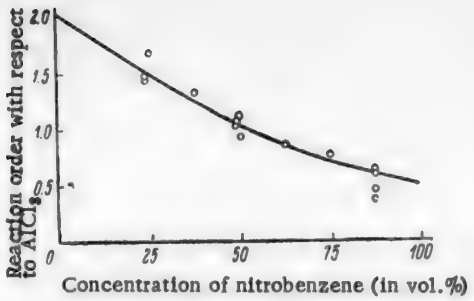

Fig. 1. Dependence of the reaction order with respect to aluminum chloride on the concentration of the solvent.

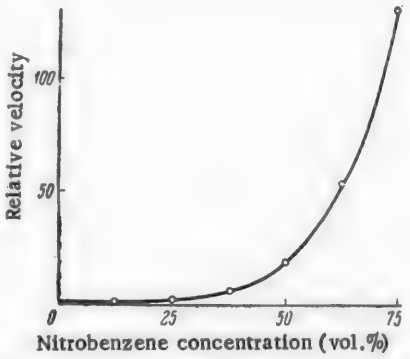

Fig. 2. Velocity of alkylation as a function of the concentration of the solvent.

These examples therefore also confirm that the order of reaction with respect to aluminum chloride decreases with increasing content of nitrobenzene in the reaction mass. All of the data obtained for the mixed solvents benzene-nitrobenzene [1] and carbon tetrachloride-nitrobenzene are plotted in Fig. 1. They vividly demonstrate the variability of the order of reaction with respect to aluminum chloride in dependence on the properties of the solvent, changing from 0.5 for nitrobenzene to 2 for benzene or carbon tetrachloride. These results again refute the conclusions of Brown and Grayson on this problem.

The results obtained suggest that for other solvents also a characteristic and different dependence of the reaction rate on the aluminum chloride concentration will be found. Corresponding experiments for the reaction of tert. butyl chloride and cyclohexyl chloride with benzene (concentration of benzene 12.5 vol.-%, Table 4) actually showed that the order of reaction with respect to aluminum chloride in carbon disulfide solution is very close to 2, but for dichloroethane it is equal to 1.0-1,38, i.e., an intermediate value previously found for a mixed solvent comprising approximately equal parts of nitrobenzene and benzene or carbon tetrachloride.

Influence of solvents on the rate of alkylation. It follows from the data of Tables 2 and 3 that the reaction rate rises sharply with increasing content of nitrobenzene in its mixtures with carbon tetrachloride. For the purpose of more convenient representation of these results, we have taken the velocity constant of the reaction of tert. butyl chloride with benzene as unity for a nitrobenzene content of 12.5 vol.-%, an aluminum chloride concentration of 0.100 mole/liter, and a temperature of 20° (Table 6), and from the data of Tables 2 and 3 we calculated the relative velocities of this reaction for other compositions of the medium. It was necessary in this connection to convert the results of experiments with tert. amyl chloride, making use of the fact that its reactivity relative to tert. butyl chloride is equal to 0.31 on the basis of experiment 5 of Table 2 and experiment 2 of Table 3. The results are plotted in Fig. 2 which shows the sharp rise of reaction velocity with increasing content of nitrobenzene in the reaction mixture. Thus, a change of its concentration from 25 to 75 vol.-% causes the reaction rate to increase 85 times, i.e., even more sharply than for mixtures of benzene with nitrobenzene.

A comparison of the different substances as solvents for the alkylation reaction is made difficult by the necessity of the presence of nitrobenzene in the reaction mass (for homogenization of the solution) as well as of benzene (the latter in excess in relation to the halogen compound). Fig. 2 nevertheless shows that with a small quantity of nitrobenzene the rate of alkylation depends on its concentration to a small extent. The effect of addition of benzene is more marked, although only when strongly ionizing solvents are used (Fig. 3 of the preceding paper [1]).

Results of the appropriate experiments with the objective of determination of the relative "activities" of solvents in alkylations, and of the energies of activation are presented in Tables 5 and 6. In all of the experiments the initial concentration of halogen compound was 0.200 mole/liter and the benzene concentration was 12.5 vol.-% (except in the experiments where it was the main solvent).

The velocity constant of alkylation in different solvents, as a function of the temperature is plotted in Figure 3. This diagram shows that the experimental points fall fairly satisfactorily on the straight line of log velocity constant versus reciprocal temperature. The energy of activation in the different solvents was calculated from the slope of the straight-line plots (Table 7).

TABLE 4

Solvent and temperature	Content of nitrobenzene (vol.-%)	Concentration of aluminum chloride (moles)	Number of parallel experiments	Velocity constant κ_1 (min^{-1})	Reaction order with respect to $AlCl_3$
		tert.-Butyl chloride + benzene			
Carbon disulfide, 20°	25.0	0.152	5	0.152 ± 3.1%	2.09
	25.0	0.100	3	0.0635 ± 1.6%	
1,1,2,2-Tetrachloroethane, 20°	12.5	0.100	4	0.198 ± 2.3%	1.6
	12.5	0.049	3	0.063 ± 0.5%	
1,2-Dichloroethane, 10°	12.5	0.049	4	0.250 ± 1.8%	1.38
	12.5	0.025	3	0.099 ± 1.6%	
		Cyclohexyl chloride + benzene			
1,2-Dichloroethane, 40°	11.0	0.100	6	0.0765 ± 1.0%	1.0
	11.0	0.049	4	0.0375 ± 1.1%	

TABLE 5

Reaction of Cyclohexyl Chloride with Benzene (Solvent: Dichloroethane, Concentration of Aluminum Chloride 0.100 Molar, Concentration of Nitrobenzene 11.0 vol.-%)

Number	Temperature	Number of parallel experiments	Velocity constant κ_1 (min^{-1})
1	25.0°	4	0.0165 ± 1.1%
2	30.0	4	0.0285 ± 1.2%
3	35.0	3	0.0475 ± 1.2%
4	40.0	6	0.0765 ± 1.0%

For comparative evaluation of the influence of the solvents on the rate of alkylation we assumed that the velocity constant of reaction of tert. butyl chloride with benzene in carbon tetrachloride solution at 20° (experiment 9, Table 6) was 1. Then from the tables and Fig. 2, also from the data of our preceding paper [1], we could calculate the relative velocities of reaction in other solvents. Due to the presence of benzene and nitrobenzene in the solution, a correction was introduced into the values obtained directly from Tables 5 and 6 in order to find the respective characteristic values for the pure solvents. The correction was found from Fig. 3 of our preceding paper [1], starting from the assumption that addition of nitrobenzene or benzene to the pure solvent has the same effect as their addition to a mixture of benzene and nitrobenzene of the same "activity" as the given solution. The relative "activities" of the solvents obtained in this fashion are shown in Table 7 together with the activation energies of the reactions and the dielectric constants of the solvents.

Comparison of the above results shows in particular the strong dependence of the rate of alkylation on the nature of the solvent, in complete contrast to the results of Brown and Grayson. This difference may be due, however, to some extent to the fact that our results were obtained with a low concentration of catalyst (0.100 molar), whereas Brown and Grayson worked with a concentration of aluminum chloride of up to 0.667 molar. The reaction rates in various solvents are therefore equalized owing to the change in the order of reaction with respect to aluminum chloride at higher concentrations of the latter.

Concerning the energies of activation, no definite relation between them and the nature of the solvent could be observed. In the case, for example, of the reaction of cyclohexyl chloride with benzene, the highest activation energy was found with active solvents, whereas in the reaction of tert. butyl chloride the opposite relation is observed. Only on comparing chemically similar solvents (chloro derivatives in this case) do we detect a slight lowering of the activation energy with increasing "activity" of the solvent. This change is insignificant, however, and it cannot account for the influence of the medium on the reaction rate. The nature of the solvent accordingly affects mainly the factor PZ of the rate equation.

TABLE 6

Reaction of Tert. Butyl Chloride with Benzene

No.	Concentration: nitrobenzene (vol. %)	Concentration: aluminum chloride (moles)	Temp. ± 0.05°	No. of parallel experiments	Velocity constant k_1 (min^{-1})
		Solvent: benzene			
1	12.5	0.100	5.0°	4	0.0390 ± 1.3%
2	12.5	0.100	10.0	3	0.064 ± 1.2%
3	12.5	0.100	15.0	4	0.107 ± 3.2%
4	12.5	0.100	20.0	4	0.169 ± 2.3%
		Solvent: carbon tetrachloride			
5	25.0	0.203	10.0	4	0.0219 ± 1.9%
6	25.0	0.203	15.0	3	0.0350 ± 1.0%
7	25.0	0.203	20.0	4	0.054 ± 1.4%
8	25.0	0.203	25.0	4	0.082 ± 1.1%
9	12.5	0.100	20.0	4	0.0104 ± 2.9%
		Solvent: carbon disulfide			
10	12.5	0.100	10.0	4	0.0145 ± 2.4%
11	12.5	0.100	15.0	3	0.0238 ± 1.6%
12	12.5	0.100	20.0	4	0.0368 ± 2.1%
13	12.5	0.100	25.0	3	0.0565 ± 1.7%
		Solvent: 1,1,2,2-tetrachloroethane			
14	12.5	0.100	5.0	4	0.049 ± 1.6%
15	12.5	0.100	10.0	4	0.079 ± 1.2%
16	12.5	0.100	15.0	3	0.121 ± 2.0%
17	12.5	0.100	20.0	4	0.186 ± 2.7%
		Solvent: 1,2-dichloroethane			
18	12.5	0.025	5.0	3	0.0645 ± 1.4%
19	12.5	0.025	10.0	4	0.099 ± 1.3%
20	12.5	0.025	15.0	3	0.151 ± 1.4%
21	12.5	0.025	20.0	4	0.218 ± 2.8%

TABLE 7

Solvent	Dielectric constant	Relative activity	Energies of activation (kcal/mole): of reaction of cyclohexyl chloride with benzene	Energies of activation (kcal/mole): of reaction of tert. butyl chloride with benzene
Carbon tetrachloride	2.24	1.0	–	14.9 ± 0.5
Benzene	2.28	2.5	17.5 ± 0.3 [1]	15.5 ± 0.3
Carbon disulfide	2.64	4.0	–	15.1 ± 0.6
1,1,2,2-Tetrachloroethane	8.0	30	–	14.4 ± 0.6
1,2-Dichloroethane	10.5	170	18.9 ± 0.5	13.2 ± 0.7
Nitrobenzene	36.1	360	18.7 ± 0.8 [1]	–

Comparison of the activity of solvents during alkylation with their dielectric constants throws some light on the mechanism of the influence of solvents. It is already evident from the data of the last table that the changes in these two parameters follow the same trend. A plot of the logarithm of the "activity" of the solvent against the reciprocal of the dielectric constant gives a straight line (Fig. 4) except in the case of tetrachloroethane for which the deviation is appreciable. A similar dependence was previously observed by Wynne-Jones [4] for the ionization constants of carboxylic acids. We are therefore forced to the conclusion that in our case the solubility influences the degree of ionization of one of the components of the reaction, namely the catalytic complex of aluminum chloride with nitrobenzene.

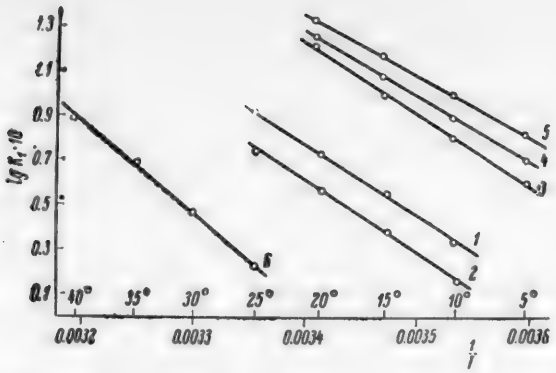

Fig. 3. Reaction velocity as a function of the temperature in the case of different solvents. For tert. butyl chloride: 1) carbon tetrachloride, 2) carbon disulfide, 3) benzene, 4) 1,1,2,2-tetrachloroethane, 5) 1,2-dichloroethane; for reaction with cyclohexyl chloride: 6) 1,2-dichloroethane.

Evaluation of Results

The general kinetic equation of catalysis with the help of aluminum chloride that we derived in the preceding paper [1],

$$-\frac{dx}{dt} = \{k_i [Al_2Cl_6]^{0.5} + k_m [Al_2Cl_6]^2\} [RCl] [ArH]$$

is fully confirmed in the present investigation. The interplay of the ionic and the molecular mechanism of catalsis and the resulting variation in the orders of the reaction with respect to aluminum chloride are characteristic features of the action of this catalyst. Here the ionic catalysis is brought about by a cation and the molecular action by the undissociated molecule of the catalytic complex. For the interpretation of the mechanism of both types of catalysis, it is necessary to remember that simultaneous triple collisions between the reaction components occur very rarely. The reaction must therefore involve some bimolecular steps. For the ionic catalysis the first of these is interaction of the cation with the halogen compound which is an equilibrium step:

$$K^+ + RCl \overset{K_h}{\rightleftarrows} K^+\overset{\delta-}{Cl} \longleftarrow \overset{\delta+}{R}$$

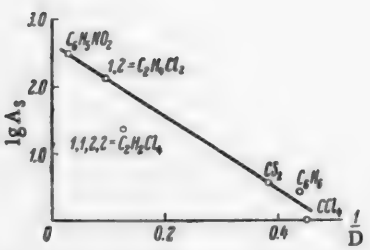

Fig. 4. Dependence of the "activity" of solvents on their dielectric constant.

In the resulting reaction complex the carbon-halogen bond is polarized to a sufficient extent for initiation of the subsequent reaction with benzene. We do not assume, however, that this bond is fully ruptured with formation of carbonium ions. Criticisms of these ideas were already noted in our previous papers [3], and they have recently been joined by those of some American authors [2, 6].

The second step of the reaction is bimolecular interaction of the reaction complex with the hydrocarbon, which we visualize (contrary to the theory of Brown and Grayson) as a true replacement of the hydrogen atom by its gradual displacement by the alkyl group which carries a partial positive charge:

$$K^+\overset{\delta-}{Cl} \leftarrow \overset{\delta+}{R} + ArH \rightleftarrows \left[K^+\overset{\delta-}{Cl}\cdots\overset{\delta+}{R}\cdots\overset{\delta-}{Ar}\cdots\overset{\delta+}{H}\right] \xrightarrow{k_2'} K^+ + HCl + ArR$$

Since the over-all rate of the process must be determined by the last reaction, we obtain the following kinetic equation:

$$-\frac{dx}{dt} = k_2'[K^+ClR][ArH] = k_2' \cdot K_h[K^+][RCl][ArH]$$

Bearing in mind that a cation is formed by dissociation of the catalytic complex [1]

$$[(C_6H_5NO_2)_2AlCl_2][AlCl_4] \overset{K}{\rightleftarrows} [(C_6H_5NO_2)_2AlCl_2]^+ + [AlCl_4]^- = K^+ + A^-,$$

we have at a low degree of dissociation:

$$[K^+] = \sqrt{K_k[Al_2Cl_6]}$$

Finally, we therefore obtain:

$$-\frac{dx}{dt} = k_2' \cdot K_k\sqrt{K_k}\,[Al_2Cl_6]^{0.5}[RCl][ArH] = k_i\,[Al_2Cl_6]^{0.5}[RCl][ArH],$$

which is also observed for the reaction in nitrobenzene solution, where k_i is the velocity constant of the ionic catalytic process.

According to Moelwyn-Hughes [7] the velocity constant of a second-order reaction is determined by the number of collisions between activated molecules, the factor P of the rate equation being equal to unity, as he showed for a number of reactions. For the reaction of cyclohexyl chloride with benzene in nitrobenzene we then obtain:

$$k_2' = PZ \cdot e^{-\frac{E}{RT}} = 1 \cdot 2.8 \cdot 10^{11} \cdot e^{-\frac{18700}{R \cdot 303}} = 9 \cdot 10^{-3}\ \text{l/mole} \cdot \text{sec} = 0.53\ \text{l/mole} \cdot \text{min}$$

The following velocity constant was found [1] experimentally for this reaction with an aluminum chloride concentration of 0.1 molar:

$$k_2 = \frac{k_1}{[C_6H_6]} = \frac{0.047}{1.408} = 0.0334\ \text{l/mole} \cdot \text{min}$$

From this we obtain:

$$k_2'K_h\sqrt{K_k}\,[Al_2Cl_6]^{0.5}[RCl][ArH] = k_2[RCl][ArH]$$

and

$$K_h\sqrt{K_k} = \frac{k_2}{k_2'[Al_2Cl_6]^{0.5}} = \frac{0.0334}{0.53\ (0.05)^{0.5}} = 0.28.$$

Since it was previously shown [8] that the reactivity both of halogen derivatives and aromatic compounds depends only on the changes in the activation energies of these reactions, the structure of the organic compounds only influences the factor $e^{-E/RT}$ which governs the number of effective collisions. On the other hand, solvents with a weak action (as shown above) on the activation energy, manifest their action by a change of the magnitude of $K_h\sqrt{K_k}$ and in particular of the equilibrium constant during dissociation of the catalytic complex K_k. This effect also determines the dependence of the influence of solvents on their dielectric constant. Consequently, the value of $K_h\sqrt{K_k} = 0.28$ must be constant for a given composition of medium and independent of the structure of the reacting organic compounds.

In the case of molecular catalysis, which predominates in weakly dissociated solvents, the halogen compound is activated by the undissociated molecule of the catalytic complex:

$$K^+A^- + RCl \overset{K'_h}{\rightleftarrows} A^-K^+\overset{\delta-}{Cl} \leftarrow \overset{\delta+}{R}$$

Due, however, to the lower strength of its electric field (relative to that created by the ion) the polarization of the carbon-halogen bond proves to be insufficient for direct reaction with benzene. The latter must also be activated by a second molecule of the dipole:

$$K^+A^- + \bigcirc \overset{K_u}{\rightleftarrows} K^+A^-\bigcirc^{\delta-}$$

The rate-determining process is the bimolecular interaction of the resulting complexes:

$$A^-K^+ClR + \bigcirc A^-K^+ \xrightarrow{k''_2} 2K^+A^- + HCl + C_6H_5R$$

In this event we obtain the kinetic equation:

$$-\frac{dx}{dt} = k''_2\,[K^+A^-RCl]\,[K^+A^-C_6H_6] = k''_2K'_h[KA][RCl]\cdot K_u[KA][C_6H_6] =$$

$$= k''_2\cdot K'_h\cdot K_u[Al_2Cl_6]^2[RCl][ArH] = k_m[Al_2Cl_6]^2[RCl][ArH],$$

which is also observed for reaction in weakly ionized solvents; where k_m is the rate constant of the molecular catalytic reaction.

Previously we found $k_2 = 0.0074$ liter/mole. min. and E = 14.7 kcal/mole for the reaction of tert. butyl chloride with benzene in carbon tetrachloride solution at 20° and a concentration of 0.1 molar $AlCl_3$. Hence, by a similar procedure we obtain:

$$k''_2 = 2.8\cdot 10^{11}\cdot e^{-\frac{14700}{R\cdot 293}} = 3.5\ 1/\text{mol. sec} = 210\ 1/\text{mol. min}$$

$$K'_h\cdot K_u = \frac{k_2}{k''_2\,[Al_2Cl_6]^2} = \frac{0.074}{210\,(0.05)^2} = 0.014.$$

This value is considerably lower than that for the ionic reaction. Molecular catalysis is therefore slower than ionic catalysis, mainly due to the considerable decrease in the equilibrium constants during formation of reaction complexes, in particular unstable complexes with hydrocarbons.

Our proposed mechanism of alkylation in presence of aluminum chloride is not limited to solutions containing nitrobenzene. This catalyst is known to give complex compounds with many organic compounds all of which carry the electric current [9]. Their formation may be a critical factor in the acceleration of a reaction, due to catalysis by the cation of these complexes, and this would also explain the high activity of Gustavson complexes (the lower layers formed during the alkylation) which are likewise ionized compounds [10]. Conversely, the poor activity of solid aluminum chloride is determined by its molecular crystalline lattice and the resulting slow molecular catalysis, which changes into the rapid ionic process as the Gustavson complexes are gradually formed.

Walker [11] also attempted to correlate the catalytic activity of aluminum chloride with ionization; he did not realize, however, that a part is here played not only by the electrical conductivity but also by the structure of the positively charged ion which depends on the structure of the organic component; the latter determines the catalytic activity of the ion itself. We know, for instance, that in complexes with ketones the catalyst is completely deactivated in spite of the ionization.

The dual mechanism of catalysis during alkylation in presence of aluminum chloride has an interesting analogy in the characteristics of catalytic action of acids in many organic reactions [12]. Thus, the fractional order of the reaction with respect to aluminum chloride, corresponding to the law of dilution of weak electrolytes, has a parallel in the case of catalysis with the hydrogen ion [13]. The kinetic equation that we derived, in which the catalytic coefficient consists of two components, corresponds to an analogous equation for acid catalysis [14] in which not only the hydrogen ion but also the undissociated molecule of acid is catalytically active. In this respect our data are consistent with the dualistic theory of acid catalysis, so that we can regard reactions in presence of aluminum chloride as one case of general acid catalysis. This interpretation is supported by the fact that suitable catalysts for alkylation reactions are not only electron acceptors of the type of metallic halides, but also a whole series of mineral acids.

SUMMARY

1. It was confirmed that the order of the alkylation of aromatic compounds with halogen-containing compounds with respect to aluminum chloride varies in dependence on the type of solvents; the latter also have a marked influence on the reaction rate. The data of Brown and Grayson on this problem are refuted.

2. The theory of the ionic and molecular mechanisms of aluminum chloride-catalyzed reactions is further developed.

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STEREOCHEMICAL INVESTIGATIONS

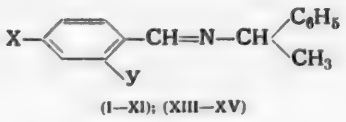
III. SCHIFF BASES FROM OPTICALLY ACTIVE α-PHENYLETHYLAMINE

A. P. Terent'ev and V. M. Potapov

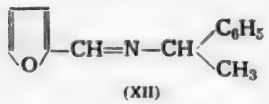
The literature contains relatively little information about optically active Schiff bases. Betti [1] described a series of such substances derived from (+)-α-(β-naphthol)-benzylamine. He had previously obtained several products of condensation of optically active α-(p-anisyl)-ethylamine with substituted benzaldehydes [2]. Several Schiff bases from isomeric methylamines [3, 4] and fenchylamine [4, 5] have also been described.

In the course of an investigation of derivatives of optically active α-phenylethylamine, we prepared a series of Schiff bases (I-XVI) from this amine.

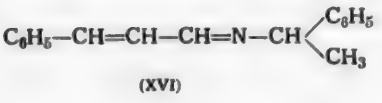
Data for these bases are given in the table. After this work had been completed and the results prepared for publication, a paper was published by Nerdel and others [6] which described several Schiff bases from (−)-α-phenylethylamine, including 4 of our preparations (II, V, VII, XI). Nerdel measured the optical activity in benzene, alcohol, chloroform and dioxane, whereas we performed the measurements in benzene, methanol, acetone and dichloroethane. Consequently, the data overlap only for the benzene solutions (the agreement was generally good); in other respects the two papers supplement one another.



(I—XI); (XIII—XV)



(XII)

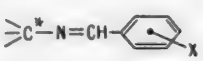


(XVI)

№	X	y
(I)	AsO_3H_2	H
(II)	H	H
(III)	iso -C_3H_7	H
(IV)	CH_3	H
(V)	OCH_3	H
(VI)	NO_2	H
(VII)	Cl	H
(VIII)	Br	H
(IX)	NH_2	H
(X)	$-OCH_2O-$	H
(XI)	$N(CH_3)_2$	H
(XIII)	H	OCH_3
(XIV)	H	OH
(XV)	H	NO_2

Examination of the table reveals a considerable divergence between the experimental and calculated values of molecular refraction; this, however, is not unexpected, since according to Auwers [7] the exaltation of molecular refraction of benzylideneamines may be as much as four units.

The tabulated data for optical activity are of particular interest for the evaluation of the influence of the nature of the substituent in the aromatic ring on the magnitude of the optical rotation in a system of the type of



Schiff Bases from (+)-α-Phenylethylamine

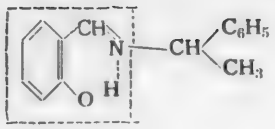
Substance number	Temperature of melting	Temperature of boiling (pressure in mm)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Yield %	Empirical formula	Found % C	Found % H	Found % N	Calculated % C	Calculated % H	Calculated % N	Molecular rotation in solvents: benzene	methanol	acetone	dichloroethane
(I)	79°	—	—	—	—	—	96	$C_{18}H_{16}O_3NAs$	—	—	4.22	—	—	4.21	—	—83°	—	—
(II)	—	161—163° (9)	1.1025	1.5888	68.8	67.3	92	$C_{18}H_{15}ON$	86.07	7.18	6.79	86.12	7.23	6.69	—168°	—160	—188°	—154°
(III)	22	194—196 (7)	0.9825	1.5621	83.0	81.1	88	$C_{18}H_{21}N$	—	—	5.28	—	—	5.36	—184	—146	—184	—164
(IV)	91—93	—	—	—	—	—	94	$C_{18}H_{17}N$	—	—	6.31	—	—	6.28	—234	—179	—229	—189
(V)	—	198 (6)	1.0635	1.5973	76.7	73.5	58	$C_{18}H_{17}ON$	—	—	5.76	—	—	5.85	—248	—219	—263	—220
(VI)	Oil														—271	—223	—254	—221
(VII)	76	—	—	—	—	—	93	$C_{18}H_{14}NCl$	73.42	5.79	—	73.96	5.79	—	—258	—190	—200	—182
(VIII)	89—90	—	—	—	—	—	78	$C_{18}H_{14}NBr$	—	—	5.08	—	—	4.85	—270	—235	—271	—217
(IX)	95—97	—	—	—	—	—	81	—	—	—	—	—	—	—	—314	—330	—390	—294
(X)	84	198—200 (4)	1.1495	1.5940	74.7	74.1	87	$C_{19}H_{19}O_2N$	—	—	5.32	—	—	5.51	—375	—327	—371	—336
(XI)	—	—	—	—	—	—	74	$C_{19}H_{20}N_2$	—	—	11.11	—	—	11.10	—460	—463	—457	—436
(XII)	—	151—154 (9)	1.0681	1.5788	62.0	61.6	85	$C_{19}H_{19}ON$	—	—	6.73	—	—	7.03	—132	—200	—216	—168
(XIII)	101	178—181 (4)	1.0573	1.5894	76.3	73.5	62	$C_{19}H_{17}ON$	—	—	5.80	—	—	5.85	+ 85	+ 74	+ 16	+ 17
(XIV)	76	—	—	—	—	—	84	$C_{19}H_{19}ON$	79.30	6.89	6.75	79.64	7.13	6.19	+ 402	+ 433	+ 330	+ 341
(XV)	168—169	(2)	1.1651	1.5970	74.4	72.3	83	—	—	—	—	—	—	—	+227	+129	+ 59	+106
(XVI)	22	—	—	—	—	—	—	—	—	—	—	—	—	—	— 23	+ 13	— 38	+ 6

The first point that is raised by the data in the table is as follows: whereas Betti had started from α-(β-naphthol)-benzylamine and obtained Schiff bases with a sign of rotation identical with that of the original amine, in the case of Schiff bases from α-phenylethylamine their sign of rotation is opposite that of the original amine. Moreover, the data in the table do not reveal the dependence on the "electronegative" or "electropositive" character of the substituent that Betti inferred from his measurements. In our case, benzaldehyde with any substituent in the para-position to the aldehyde group gives a Schiff base whose molecular rotation is higher than that of the product of condensation with unsubstituted benzaldehyde. This forces us to the conclusion that the action of the substituent on the magnitude of rotation cannot be explained solely as an electronic effect. This conclusion is strengthened on consideration of the data obtained for compounds of the ortho-series. If the sole decisive factor had been the electronic influence of the substituent transmitted along the conjugated chain to the asymmetric center, then the magnitude of the rotation for compounds containing a substituent in the ortho-position should not appreciably differ from the rotation of the analogous para-compounds. Furthermore, experimental data reveal the characteristic behavior of compounds of the ortho-series. Whereas all of the compounds of the para-series are characterized by a high molecular rotation whose sign is opposite to that of the original amine, the sign of the rotation of the original amine is retained in the case of ortho-methoxy (XIII) and ortho-nitro (XV) derivatives on transition to the corresponding Schiff base. These two compounds are distinguished by a high dependence of the magnitude of rotation on the solvent. The same is true of the Schiff bases from furfural and cinnamaldehyde.

An insight into the causes of the unusual behavior of ortho-substituted derivatives may be obtained by using models to examine the possibility of free rotation round the single bonds present in the system*. Such considerations indicate the possibility of formation by ortho-compounds of preferred configurations (rotational isomers) due to steric hindrance round the bond between the substituted benzene ring and the -CH=N- group. Since the formation of a hydrogen bond -O-H·····N is very probable for salicylal-α-phenylethylamine (XIV), the preferred configuration in this case must probably be

* In another paper [8] we considered the role of rotational isomerism with reference to the literature and to our own experiments.

Here the whole of the group enclosed in the dashed frame must be visualized as fixed in the plane of the diagram.



In the case of the ortho-methoxy derivative, for which the formation of a similar hydrogen bond is impossible and in which at the same time the bulkier OCH_3 group opposes the formation of a "plane" rotational isomer, the "nonplanar" configurations are precisely the ones that will be preferred. This also applies to the ortho-nitro- derivative, and thus accounts for the considerable difference between the optical rotations of these two Schiff bases in comparison with the salicylal derivative.

It is also evident that the nature of the solvent will have a profound effect on the stability of one or the other of the rotational isomers resulting from intramolecular interaction of the groups. This provides an explanation of the great dependence of the magnitude of rotation on solvents which is observed for compounds (XIII) and (XV) (for obvious reasons this does not apply to the "fixed" hydrogen bond of the salicylal derivative). Similarly we account for the analogous strong dependence in the case of (XII), since the α-furyl residue is also a characteristic "nucleus with an ortho-substituent". A similar explanation may also be offered for Nerdel's observation [6] of the great dependence of $[\alpha]_D$ on the solvents in the case of naphthal-α-phenylethylamine and the Schiff base from the same amine and pyridine-3-aldehyde.

EXPERIMENTAL

α-Phenylethylamine was prepared by reductive amination of acetophenone by the Leuckart method [9]. It was resolved into the optical antipodes with acid borneol sulfate [10] or tartaric acid in methanol [11]. Successive employment of both methods affords the possibility of convenient preparation of the dextro- as well as the levoratatory amine.

Racemic benzal-α-phenylethylamine. To 21.2 g of freshly distilled benzaldehyde was gradually added a solution of 24.2 g of DL-α-phenylethylamine in 60 ml of benzene, and the mixture was refluxed for an hour. The benzene and the water of reaction were then distilled off, and the residue was distilled in vacuo. Yield 27 g (65%).

B. p. 161-163° (9 mm), d^{20}_4 1.025, $n^{20}D$ 1.5888, MR_D 68.79; calculated 67.27.

Kann and Tafel [12] also prepared this substance and report b. p. 273-275° (14 mm); they did not give other constants. The erroneous boiling point was also entered in Beilstein [13].

Benzal-(+)-α-phenylethylamine (II). The procedure was the same as for the preceding preparation, starting from benzaldehyde and (+)-α-phenylethylamine in 35 ml of methanol. Constants for this and other Schiff bases from optically active α-phenylethylamine and data for their molecular rotation appear in the table. In the case of other substances we shall report only the values found for specific rotations which serve as a basis for the calculation of the magnitude of $[M]_D$.

$[\alpha]^{18}D$ −83.2° (without solvent, *l* 1.0); −80.3° (benzene, c 7.7); −76.6° (methanol, c 5.0); −00.1° (acetone, c 4.3); −73.4° (dichloroethane, c 4.1).

p-Isopropylbenzal-(+)-α-phenylethylamine (III). Prepared on the same lines as the preceding compound from (+)-α-phenylethylamine and freshly distilled cumnal without a solvent.

$[\alpha]^{20}D$ −73.2° (benzene, c 10.0); −58.3° (methanol, c 7.2); −73.1° (acetone, c 5.3); −65.5° (dichloroethane, c 3.5).

p-Methoxybenzal-(+)-α-phenylethylamine (V). Prepared as above from (+)-α-phenylethylamine and freshly distilled anisaldehyde.

$[\alpha]^{20}D$ −103.5° (benzene, c 8.0); −91.5° (methanol, c 5.1); −109.8° (acetone, c 5.0); −93.4° (dichloroethane, c 3.8).

Piperonal-(+)-α-phenylethylamine (X). Prepared as above from (+)-α-phenylethylamine and piperonal.

$[\alpha]^{20}D$ −148.4° (benzene, c 7.5); −129.0° (methanol, c 4.5); −146.2° (acetone, c 4.8); −132.5° (dichloroethane, c 2.2).

Furfural-(+)-α-phenylethylamine (XII). Prepared from equivalent quantities of (+)-α-phenylethylamine and freshly distilled furfural. Condensation was effected by 4-days' standing at room temperature. The constants of the prepared compound are identical with those reported in the paper by Nerdel and others, but our value for the optical activity was considerably higher than that of the authors cited.

$[\alpha]^{20}D$ −96.0° (without solvent, *l* 1.0); −66.1° (benzene, c 6.4); −100.6° (methanol, c 4.8); −108.3° (acetone, c 5.9); −84.2° (dichloroethane, c 2.5).

o-Methoxybenzal-(+)-α-phenylethylamine (XIII). Prepared from equimolar quantities of (+)-α-phenylethylamine (not completely resolved – optical purity 59.5%) and o-methoxybenzaldehyde by condensation on prolonged standing at room temperature. A parallel experiment was run with α-phenylethylamine of 100% optical purity; the reaction product was not distilled; the water was removed by aspiration in vacuo on a water bath and the oily residue was used directly for the polarimetric measurements. The agreement between the two sets of results showed that the use of the amine in a state of incomplete optical purity was permissible and that the undistilled product of condensation could be used for exploratory determinations of $[\alpha]_D$ (error of the order of ± 0.5°).

$[\alpha]^{20}D$ +79.3° (benzene, c 10.0); +70.0° (methanol, c 3.6); +15.4° (acetone, c 3.3); +15.8° (dichloroethane, c 2.5)*.

o-Nitrobenzal-(−)-α-phenylethylamine (XV). Prepared by condensation of equimolecular quantities of (−)-α-phenylethylamine** and o-nitrobenzaldehyde.

$[\alpha]^{20}D$ −78.2° (without solvent, *l* 1.0); −89.5° (benzene, c 7.5); −60.9° (methanol, c 3.5); −23.1° (acetone c 4.7); −41.4° (dichloroethane, c 1.7).

Schiff base from (−)-α-phenylethylamine and cinnamaldehyde (XVI). A mixture of equimolecular quantities of freshly distilled cinnamaldehyde and (−)-α-phenylethylamine was left for 1 hour on a warm water bath; the water of reaction was removed by aspiration in vacuo; the residue crystallized on standing in a refrigerator. Due to the low melting point (about 22°), the crystals could not be purified by recrystallization. Determinations were therefore carried out on a product washed with the minimum quantity of ether and dried in vacuo.

$[\alpha]^{20}D$ −26.3°(without solvent, *l* 1.0); 9.7° (benzene, c 3.0); −5.3° (methanol, c 3.3); 16.1° (acetone, c 1.8); −2.7° (dichloroethane, c 1.2).

Salicylal-(−)-α-phenylethylamine (XIV). A mixture of 12.23 g of freshly distilled salicylaldehyde and 13.0 ml of (−)-α-phenylethylamine in 20 ml of methanol was heated for 30 minutes on a water bath; a picric-yellow precipitate came down on cooling and was recrystallized from methanol. Yield 19.0 g (84%).

$[\alpha]^{20}D$ +202° (methanol, c 2.1); +187° (benzene, c 2.2); +147° (acetone, c 2.7); +151° (dichloroethane, c 1.5).

p-Dimethylaminobenzal-(−)-α-phenylethylamine (XI). This was prepared on the same lines as the preceding compound, starting from (−)-α-phenylethylamine and p-dimethylaminobenzaldehyde.

$[\alpha]^{20}D$ +182.5° (benzene, c 7.4); +183.4° (methanol, c 3.6); +181.4° (acetone, c 6.3); +172.8° (dichloroethane, c 2.4).

p-Aminobenzal-(−)-α-phenylethylamine (IX). Prepared from (−)-α-phenylethylamine and p-aminobenzaldehyde by the same procedure.

$[\alpha]^{20}D$ +140.2° (benzene, c 3.8); +143.8° (methanol, c 4.2); +174.0 (acetone, c 3.4); +131.1° (dichloroethane, c 2.0).

p-Chlorobenzal-(−)-α-phenylethylamine (VII). Prepared from (−)-α-phenylethylamine and p-chlorobenzaldehyde as above.

$[\alpha]^{20}D$ +106° (benzene, c 2.4); +77.5° (methanol, c 2.0); +81.8° (acetone, c 1.8); +74.6° (dichloroethane, c 1.0).

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* All values of $[\alpha]_D$ recalculated for optically pure product.

** The experimental values are given with the opposite sign in the table in all cases when (−)-α-phenylethylamine was used.

p-Bromobenzal-(−)-α-phenylethylamine (VIII). Prepared analogously to the preceding compound from (−)-α-phenylethylamine and p-bromobenzaldehyde.

$[\alpha]_D^{20}$ +93.5° (benzene, c 1.9); +81.6° (methanol, c 2.0); +94.0° (acetone, c 2.4); +75.7° (dichloroethane, c 1.7).

p-Tolyl -(+)-α-phenylethylamine (IV). Prepared analogously to the preceding compound from (+)-α-phenylethylamine and p-tolylaldehyde.

$[\alpha]_D^{20}$ −104.8° (benzene, c 6.1); −80.2° (methanol, c 4.2); −102.6° (acetone, c 4.2); −84.8° (dichloroethane, c 3.1).

p-Arsinacidobenzal-(−)-α-phenylethylamine (I). Prepared from (−)-α-phenylethylamine and benzaldehyde-p-arsinic acid on the same lines as the previous preparation.

$[\alpha]_D^{20}$ +24.8° (methanol, c 3.1); −1.5° (water, c 2.9); +39.7° (0.7% aqueous NaOH solution). No determinations of $[\alpha]_D$ were made in the other solvents due to the poor solubility of the substance.

p-Nitrobenzal-(−)-α-phenylethylamine (VI). Prepared by condensation of (−)-α-phenylethylamine with p-nitrobenzaldehyde on a water bath; water of reaction was removed by aspiration in vacuo. Rotations were measured on the undistilled condensation product.

$[\alpha]_D^{20}$ +106.4° (benzene, c 6.2); +88.3° (methanol, c 4.2); +100.0° (acetone, c 4.0); +87.0° (dichloroethane, c 1.8).

SUMMARY

1. Schiff bases were prepared from optically active α-phenylethylamine and benzaldehyde, 13 substituted benzaldehydes, cinnamaldehyde and furfural.

2. Optical activities of the prepared Schiff bases were determined in benzene, methanol, acetone and dichloroethane.

3. The results are utilized for clarification of the problem of the possible influence of rotatory isomerism on the magnitude of the rotation.

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PREPARATION OF α-AMINOACIDS VIA FURAN DERIVATIVES

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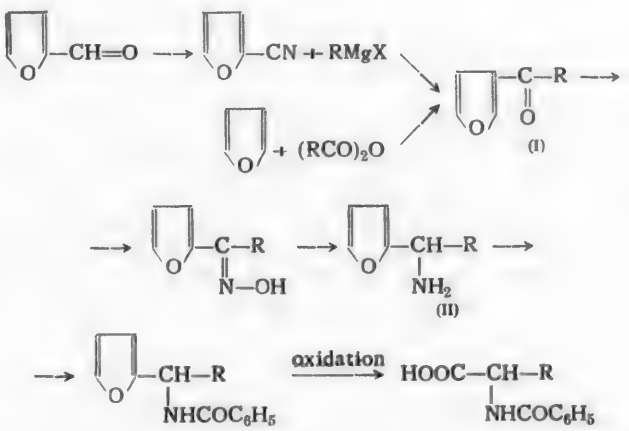
With the aim of verifying the structure of 2-methyl-1-furylcyclopropane that he had prepared, N. M. Kizhner [1] subjected it to oxidation with potassium permanganate. In this way the furan ring was converted into carboxyl, a yield of up to 77% of 2-methylcyclopropanecarboxylic acid being obtained. V. F. Kucherov [2] performed a similar oxidation to verify the structure of butyl and isobutyl furyl carbinols (in the form of ethyl ethers).

The facility of transformation of the furan ring into carboxyl indicated the possibility of utilizing this reaction for the synthesis of derivatives of carboxylic acids.

Furfural and furan are not only readily accessible, but can be used as starting substances for diverse derivatives. Many syntheses of furylketones from furan have been described on the basis of reactions of the Friedel-Crafts type with acid chlorides and anhydrides. Furfural easily gives 2-furoic acid, or (via the oxime) 2-furonitrile. The latter can be transformed into various ketones by reaction with organomagnesium compounds. On this basis, we decided to exploit the reactivity of furans for synthesis of α-aminoacids containing the furan ring as the potential carboxyl.

The following reaction schemes are involved:



It should be noted that the amines serving as intermediates in this sequence of reactions are themselves of definite interest; only a few representatives of this group have been studied.

We applied the above-described transformations to three compounds (R = CH_3, C_3H_7, n-C_4H_9). Acetylfuran was prepared from furan and acetic anhydride in presence of phosphoric acid [3]; propyl and butyl furyl ketones were prepared from 2-furonitrile by the Grignard reaction [4]. Yields of ketones 60-70%. Reduction of the oximes of the ketones to the corresponding amines with zinc and acetic acid gives yields of 50-60%. Oxidation of the benzoyl derivatives of the amines was effected with potassium permanganate in an alkaline medium. In this fashion we obtained the benzoyl derivatives of three aminoacids – alanine, norvaline and norleucine – in yields of 50-70%.

EXPERIMENTAL

Alkyl-α-Furyl Ketones (I)

n-Butyl and propyl furyl ketones. Furonitrile (0.4 mole) in absolute ether was added (with stirring and cooling) to the Grignard reagent prepared from 0.5 mole alkyl bromide and 0.5 mole magnesium in absolute ether. The reaction mass was left overnight and then decomposed with 10% hydrochloric acid. The ketone was extracted with ether and dried. After the solvent had been driven off, the ketone was distilled in vacuo.

For preparation of the oxime, the ketone (0.1 mole) was dissolved in 50 ml of 95% alcohol and mixed with an aqueous solution of 0.2 mole of hydroxylamine hydrochloride and 0.2 mole of potassium carbonate. The mixture was boiled for 3 hours on an oil bath. After cooling, the alcohol was distilled off in vacuo and the oxime was extracted with ether.

n-Butyl furyl ketone. Yield 60%. B. p. 100-101° (10 mm), n_D*1.4929.

Oxime. Yield 85%, b. p. 131-132° (10 mm).

Found %: N 8.03. $C_9H_{13}O_2N$. Calculated %: N 8.38.

Propyl furyl ketone. Yield 60%, b. p. 96° (20 mm), $n^{16}D$ 1.4992.

Oxime. Yield 90%, b. p. 119° (10 mm).

Found %: C 62.58, 62.47; H 7.43, 7.28. $C_8H_{11}O_2N$. Calculated %: C 62.72; H 7.23.

Acetylfuran was prepared by heating 1 mole of furan, 2 moles of acetic anhydride and 20 g of phosphoric acid on a water bath at 60-70° for 2 hours. After cooling, the reaction mass was decomposed with water and neutralized with sodium carbonate. The ketone was extracted with ether. Yield of acetylfuran 70%, b. p. 74° (22 mm) [3], b. p. 66-68° (11-12 mm) [3].

Acetylfuran oxime was prepared as described above. After the ether had been driven off, the oxime was filtered. Yield 90%, m. p. 94-95°.

Found %: C 57.55, 57.74; H 5.77, 5.73; N 11.29, 11.35. $C_6H_7O_2N$. Calculated %: C 57.59; H 5.64; N 11.19.

Amines (II)

25 g of zinc dust was added to a solution of 0.1 mole of alkyl furyl ketone oxime in 100 ml of methyl alcohol. Acetic acid (50 g) was slowly stirred dropwise into the reaction mass. Heat was developed and the mixture turned light yellow. After heat generation had ceased, the reaction mass was heated for 3 hours on a water bath. The acetic acid was driven off in vacuo. The residue was made alkaline and the amine was distilled off in steam. The distillate was acidified with hydrochloric acid (until acidic to Congo) and evaporated to a small volume. The product was made alkaline and the amine was extracted with ether and dried with caustic alkali. The N-benzoyl derivatives of the amines were prepared in the usual manner (treatment with benzoyl chloride in strongly alkaline solution).

1-Amino-1-(α-furyl)-ethane was obtained in 50% yield.

B. p. 145-147° (740 mm), $n^{20}D$ 1.4758, d^{20}_4 0.9856, MR_D 31.79; calculated 31.84.

Literature data [5]: b. p. 155°(752 mm), $n^{21}D$ 1.4799, d^{20}_4 1.008.

The benzoyl derivative had m. p. 89-90° (from acetone); yield 96%.

Found %: C 72.16, 72.34; H 6.18, 6.10; N 6.64, 6.59. $C_{13}H_{13}O_2N$. Calculated %: C 72.55; H 6.08; N 6.55.

1-Amino-1-(α-furyl)-butane was obtained in 60% yield.

B. p. 92° (20mm), $n^{20}D$ 1.4735, d^{20}_4 0.9583, MR_D 40.88; calculated 41.07.

Literature data [6]: b. p. 83-85° (14 mm).

The benzoyl derivative was obtained in 90% yield; m. p. 80°.

* As in original — Publisher's note.

1-Amino-1-(α-furyl)-pentane was obtained in 60% yield.

B. p. 104° (24 mm), $n^{20}D$ 1.4726, d^{20}_4 0.9494, MR_D 45.28; calculated 45.69.

Found %: C 70.93, 71.03; H 9.69, 9.88. $C_9H_{15}ON$. Calculated %: C 70.55; H 9.87.

The benzoyl derivative was obtained in 95% yield; m. p. 72° (from ligroine).

Found %: N 5.17, 5.09. $C_{16}H_{19}O_2N$. Calculated %: N 5.44.

Benzoyl Derivatives of α-Aminoacids

To a solution of 0.01 mole of benzoyl derivative of amine in 100 ml of acetone was added 1 ml of 20% potassium hydroxide, and a solution of 8.2 g of potassium permanganate in 250 ml of water was stirred in (temperature of reaction mixture not higher than 15°). After decolorization of the mass, a further 8.3 g of finely pulverized potassium permanganate was added and the mixture left overnight. The manganese dioxide was filtered off and washed with hot water; the combined filtrates were evaporated to a volume of 25 ml. Hydrogen chloride was passed into the solution; the precipitated benzoyl derivative of the aminoacid was recrystallized from water or dilute alcohol.

Benzoylalanine. Yield 50%, m. p. 163-164° (from water) [7].

Found %: N 7.23, 7.10. $C_{10}H_{11}O_3N$. Calculated %: N 7.25.

Benzoylnorvaline. Yield 60%, m. p. 151-152° [8].

Found %: N 6.14, 6.28. $C_{12}H_{15}O_3N$. Calculated %: N 6.33.

Benzoylnorleucine. Yield 70%, m. p. 131-132° (from aqueous alcohol) [9].

Found %: N 5.78, 6.07. $C_{13}H_{17}O_3N$. Calculated %: N 5.95.

SUMMARY

A method was developed for the preparation of α-aminoacids (benzoyl derivatives) which involved the following steps: α-furylketones, oximes, amines, benzoylamines, oxidation of the latter to N-benzoyl-α-aminoacids.

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SYNTHESIS OF 6,7-DISUBSTITUTED DERIVATIVES OF 1-AZABICYCLO-(3.2.1)-OCTANE

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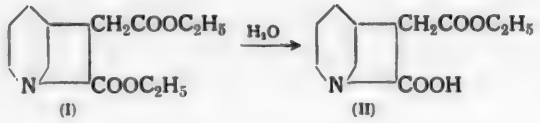
In our previous communication [1] we have described a simple method for the preparation of 6-carboxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid and of some of its derivatives.

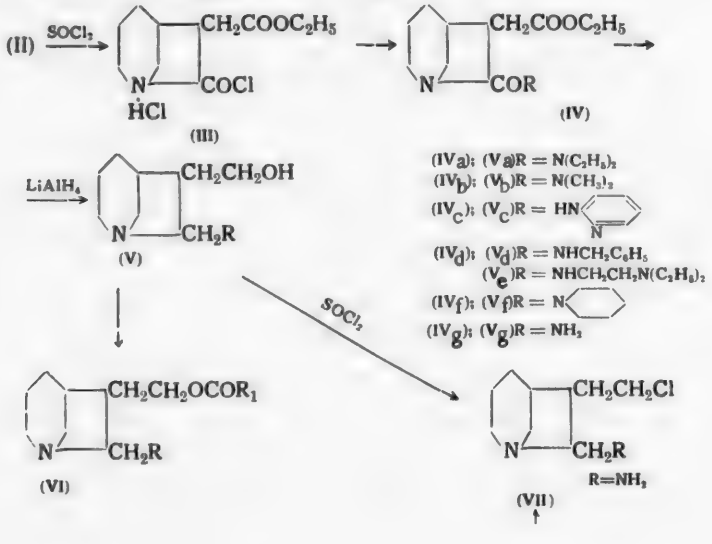
In the course of the investigation of the chemical behavior of these compounds the properties of the ethyl ester of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid were found to be of greatest interest. Thus, it was found that this diester easily undergoes hydrolysis on standing in aqueous solution, with formation of an acid ester. As has previously been pointed out [2], this property is also exhibited by the isomeric ethyl ester of 3-carbethoxymethyl-quinuclidine-2-carboxylic acid. Under similar conditions the latter ester is transformed into 3-carbethoxymethylquinuclidine-2-carboxylic acid. A comparison of the properties of these two isomeric diesters gives reason to suppose that it is the carbethoxy group in position 7 in the ethyl ester of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid (I) which undergoes hydrolysis, and the acid ester so formed has the structure of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid (II).



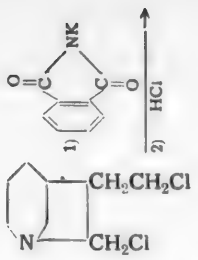
(I) (II)

Starting from the latter compound we have obtained a number of 7-alkyl-(aryl)-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes and also several esters of 7-dialkyaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane.

The syntheses were effected according to the following scheme:



(VIa) $R = N(C_2H_5)_2$ $R_1 = C_6H_5$
(VIb) $R = N(C_2H_5)_2$ $R_1 = CH_3$
(VIc) $R = N(CH_3)_2$ $R_1 = C_6H_5$
(VId) $R = N(CH_3)_2$ $R_1 = CH_3$
(VIe) $R = N(CH_3)_2$ $R_1 = CH_2CH_3$



The carboxylic acid (II) was transformed by means of thionyl chloride into the hydrochloride of the acid chloride (III) which was subsequently treated with alkyl-(aryl)-amines.

The resultant alkyl-(aryl)-amides (IV) were then reduced by means of lithium aluminum hydride to the corresponding 1-azabicyclo-(3.2.1)-octane derivatives (V). On treating the latter with certain acyl chlorides there were obtained the corresponding esters (VI). On interacting derivative (V_g) with thionyl chloride there was obtained the 7-aminomethyl-6-(β-chloroethyl) derivative (VII).

It must be pointed out that compound (VII) is also formed during the condensation of 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane, prepared earlier [1], with potassium phthalimide and the subsequent hydrolysis of the phthalimide derivative with hydrochloric acid, which indicates a restricted lability of the chlorine atom in the 6-β-chloroethyl group.

EXPERIMENTAL

Diethylamide of the carboxylic acid (II) (Compound IVa). 3 g of the ethyl ester of the carboxylic acid (II) was dissolved in 60 ml of water and the solution was allowed to stand at room temperature for 7 days. The water was then removed in vacuo and the residue dried by triple steam distillation with benzene. The acid ester obtained was washed several times with ether in order to remove any unhydrolyzed diester and was then dissolved in 50 ml of chloroform; the chloroform solution was filtered from the 6-carboxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid. After removing the chloroform in vacuo there remained 2.4 g (89%) of the carboxylic acid (II) in the form of a viscous oil. The acid ester obtained was heated, without further purification, with 30 ml of thionyl chloride for 4 hours at 60-75°. Excess thionyl chloride was removed in vacuo and the last traces were removed by triple distillation with benzene.

The foam-like mass representing the hydrochloride of 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid chloride, was suspended in 25 ml of anhydrous ether and treated with a solution of 7 g of diethylamine in 30 ml of benzene, with cooling. The reaction mixture was allowed to stand for 1 hour after which 50% potassium hydroxide solution was added and the oil which separated extracted with benzene. The benzene extract was dried over potassium hydroxide. After removing the solvent in vacuo the residue was distilled. B. p. 151-154° at 0.3 mm. In this way there was obtained 2.2 g (75%) of the diethylamide of the carboxylic acid (II) in the form of a mobile liquid which is soluble in water and organic solvents.

Found %: C 64.61, 64.83; H 9.50, 9.35; N 9.53, 9.03. $C_{15}H_{28}O_3N_2$. Calculated %: C 64.86; H 9.46; N 9.46.

Dimethylamide of the carboxylic acid (II) (Compound IVb). By interacting the carboxylic acid (II), obtained from 2.1 g of its ethyl ester by the method described in the foregoing experiment, with thionyl chloride there was obtained the acid chloride of (II). On treating the latter with 30 ml of a 15% solution of dimethylamine in ether there was obtained 1.4 g (75.5%) of dimethylamide of the carboxylic acid (II) (Compound IVb). Brown viscous liquid, b. p. 134-141°/0.2 mm, soluble in water and organic solvents.

Found %: C 62.48, 62.04; H 8.51, 8.98. $C_{14}H_{24}O_3N_2$. Calculated %: C 62.68; H 8.95.

The methiodide was obtained as white crystals soluble in water and alcohol and insoluble in ether, m. p. 178-180°.

Found %: I 30.87, 30.42; N 6.67, 6.50. $C_{15}H_{27}O_3N_2I$ Calculated %: I 30.97; N 6.83

Pyridyl-(2')-amide of the carboxylic acid (II) (Compound IVc). The hydrochloride of the carboxylic acid (II) chloride (Compound III) prepared from 2.1 g of the diester (I) by the method described above, was treated

with a solution of 4.44 g of 2-aminopyridine in 25 ml of benzene; there was obtained 1.42 g (63%) of Compound (IVc) in the form of a brown viscous liquid, soluble in water and organic solvents. B. p. 185°/0.3 mm.

The dipicrate was obtained in the form of yellow crystals which are soluble in acetone and difficultly soluble in alcohol. M. p. 188-191° (from a mixture of acetone and alcohol).

Found %: C 44.76, 44.76; H 3.69, 3.74; N 16.22, 16.22. $C_{29}H_{29}O_{17}N_9$. Calculated %: C 44.90; H 3.73; N 16.25.

Benzylamide of the carboxylic acid (II) (Compound IVd). To a mixture of compound (III) obtained from 2.1 g of the diester (I), and 25 ml of ether was added, with cooling, a solution of 5 g of benzylamine in 25 ml of benzene. After the usual treatment, described in foregoing experiment, there was obtained 2 g (87%) of compound (IVd), b. p. 178°/0.3 mm. Greenish-yellow liquid, somewhat viscous, soluble in water and organic solvents.

Found %: C 69.40, 69.42; H 7.69, 7.96; N 8.67, 8.55. $C_{19}H_{28}O_3N_2$. Calculated %: C 69.10; H 7.86; N 8.50.

N-[6-Carbethoxymethyl-1-azabicyclo-(3.2.1)-octanoyl-7]-piperidine (IVf). A mixture consisting of the hydrochloride (III), obtained from 30 g of the diester (I), 300 ml of benzene and 90 ml of piperidine was refluxed for 4 hours. Excess piperidine and solvent were removed in vacuo and the residue dissolved in 50 ml of water and treated with 50% solution of potassium hydroxide. The amide formed was extracted with benzene. After drying the benzene solution over caustic potash, the solvent was removed and the substance distilled in vacuo, b. p. 180°/0.3 mm.

The amide obtained is an oily rather viscous liquid which is soluble in organic solvents. Yield, 27.9 g (81%).

Found %: N 8.82, 8.55. $C_{17}H_{28}O_3N_2$. Calculated %: N 9.09.

Amide of carboxylic acid (II) (Compound (IVg). 14.2 g of the diester (I) was transformed into the acid chloride by the method described above. The latter was suspended in 100 ml of ether; the reaction mixture was saturated with ammonia during 1 hour, with cooling. The reaction mixture was then treated with 50% caustic potash and the amide formed extracted with benzene. After drying the benzene solution over potash and removing the solvent in vacuo there was obtained the amide (IVg) in the form of colorless crystals, m. p. 118° (from ethyl acetate), yield 2.4 g (19%).

Found %: C 60.34, 59.78; H 8.42, 8.26; N 11.74, 11.45. $C_{12}H_{20}O_3N_2$. Calculated %: C 60.00; H 8.33; N 11.66.

7-Diethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Va). A solution of 5 g of the diethylamide of the carboxylic acid (II) (Compound IVa) in 50 ml of anhydrous benzene was added to a suspension of 2.64 g of lithium aluminum hydride in 50 ml of anhydrous ether. The reaction mixture was refluxed for 20 hours. At the end of this period 5 ml of water was added with cooling and stirring. The lithium and aluminum hydroxides formed were filtered off and were thoroughly washed with ether. The extracts were dried over potassium hydroxide. After removing the solvent the residue, representing compound (Va), was distilled in vacuo, b. p. 140-143°/0.2 mm. Yield 3.25 g (80.5%). Mobile colorless liquid soluble in water and organic solvents.

Found %: N 11.44, 11.22. $C_{14}H_{28}ON_2$. Calculated %: N 11.66.

7-Dimethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vb). A solution of 2.4 g of the amide (IVb) in 30 ml of benzene was added to a suspension of 1.4 g of lithium aluminum hydride in 20 ml of ether. After refluxing the mixture for 20 hours it was treated in a manner similar to that described in the foregoing experiment. There was obtained 1.43 g (76%) of the amine (Vb) as a viscous colorless oil, soluble in water and organic solvents. B. p. 130-132°/0.3 mm.

Found %: N 12.65. $C_{12}H_{24}ON_2$. Calculated %: N 13.21.

The dipicrate was obtained as yellow crystals, soluble in alcohol and acetone; insoluble in water, benzene, ether. M. p. 64-70°.

Found %: C 42.82, 43.29; H 4.85, 4.60; N 16.68. $C_{24}H_{30}O_{15}N_8$. Calculated %: C 42.98; H 4.47; N 16.71.

The dimethiodide was obtained in the form of a white amorphous powder, soluble in water and alcohol and insoluble in ether.

Found %: N 5.92, 6.12. $C_{14}H_{30}ON_2I_2$. Calculated %: N 5.64.

7-(Pyridyl-2')-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vc). 1.2 g of the amide (IVc) was reduced with 0.6 g of lithium aluminum hydride. There was obtained 0.7 g (70.2%) of compound (Vc) as a yellow viscous liquid, easily soluble in organic solvents and water. B. p. 188-190°/0.3 mm.

The dipicrate is in the form of yellow crystals, soluble in alcohol and acetone, and insoluble in ether and water. M. p. 178-180°.

Found %: C 44.65, 44.75; H 4.05, 4.17; N 17.50. $C_{27}H_{29}O_{15}N_9$. Calculated %: C 45.06; H 4.05; N 17.52.

7-Benzylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vd). A solution of 2.1 g of the amide (IVd) in 20 ml of benzene was added to a suspension of 1 g of lithium aluminum hydride in 20 ml of ether. After heating at 60° for 20 hours 20 ml of anhydrous dioxan was added to the reaction mixture and heating was continued at reflux for another 20 hours. The reaction products were treated by the method described. There was obtained 1.4 g (80%) of Compound (Vd) as a viscous yellow oil, soluble in organic solvents and water. B. p. 194-196°/0.3 mm.

Found %: C 74.21, 74.11; H 9.31, 9.50; N 9.89. $C_{17}H_{26}ON_2$. Calculated %: C 74.45; H 9.49; N 10.21.

The dipicrate was obtained as a yellow amorphous powder, soluble in alcohol and acetone; insoluble in water, ether, benzene. M. p. 86° (decomp.).

Found %: C 47.60; H 4.60; N 15.65. $C_{29}H_{32}O_{15}N_8$. Calculated %: C 47.54; H 4.37; N 15.30.

7-Diethylaminoethylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Ve). The hydrochloride (III), prepared from 2.1 g of the diester (I), was suspended in 25 ml of ether and the suspension was added, with cooling and stirring to a solution of 5 g of diethylaminoethylamine in 25 ml of benzene. After the usual treatment (as described for Compound IVa) there was obtained 2.1 g (89%) of diethylaminoethylamide of the carboxylic acid (II) as a brown oil which decomposed on distillation. Because of the danger of decomposition the compound was reduced with lithium aluminum hydride without further purification. The crude amide was treated with 1 g of the hydride. The amine formed was extracted with chloroform. After removing the chloroform the residue was distilled in vacuo, b. p. 175°/0.15 mm. Yield, 1 g (57%) of Compound (Ve). Brown viscous oil, soluble in organic solvents and water.

Found %: N 14.92, 15.22. $C_{16}H_{33}ON_3$. Calculated %: N 14.84.

N-[7-(β-Hydroxyethyl)-1-azabicyclo-(3.2.1)-octanomethyl-6]-piperidine (Vf). A solution of 25 g of the amide (IVf) in 250 ml of benzene was added to a suspension of 12.3 g of lithium aluminum hydride in 250 ml of benzene. The reaction mixture was refluxed for 20 hours. The amino alcohol formed was extracted with benzene, yield 17 g (85%). The substance is a yellow viscous oil easily soluble in organic solvents and water. B. p. 156-157°/0.3 mm.

Found %: N 10.96, 10.68. $C_{15}H_{28}ON_2$. Calculated %: N 11.11.

7-Aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octane (Vg). 1.5 g of the amide (IVg) was added portion-wise to a suspension of 0.49 g of lithium aluminum hydride in a mixture of 30 ml of benzene and 20 ml of ether. The reaction mixture was treated as above, yielding 0.45 g (59%) of the amino alcohol (Vg) as a viscous liquid, soluble in organic solvents and water, b. p. 140°/0.3 mm.

The dipicrate was obtained as yellow crystals, soluble in alcohol, acetone; insoluble in water and ether. M. p. 87°.

Found %: C 41.33; H 4.36. $C_{22}H_{26}O_{15}N_8$. Calculated %: C 41.10; H 4.05.

7-Diethylaminomethyl-6-(β-benzoylhydroxyethyl)-1-azabicyclo-(3.2.1)-octane (VIa). To a solution of 1.5 g of the amino alcohol (Va) in 15 ml of anhydrous benzene was added, with cooling, 1.2 ml of benzoyl chloride. The reaction mixture was refluxed for 3 hours. The dihydrochloride of (VIa) formed was extracted from its solution in benzene with 5% hydrochloric acid. The hydrochloric acid solution was made alkaline with

50% potassium hydroxide solution and the base (VIa) extracted with ether. After drying the ether extract over potassium hydroxide and removing the solvent, the substance was distilled in vacuo, b. p. 189°/0.4 mm. Yield 1.6 g (76%). Light-yellow oil, easily soluble in organic solvents $n^{18}D$ 1.5285.

Found %: C 72.42, 72.52; H 9.26, 9.17; N 8.36, 7.93. $C_{21}H_{32}O_2N_2$. Calculated %: C 72.92; H 9.3; N 8.11.

7-Diethylaminomethyl-6-(β-acetoxyethyl)-1-azabicyclo-(3.2.1)-octane (VIb). A mixture consisting of 1.9 g of compound (Va), 0.7 g of acetyl chloride and 20 ml of benzene was refluxed for 3 hours. Excess acetyl chloride and solvent were removed in vacuo and the residue – the dihydrochloride of (VIb) – was dissolved in water. The solution was made alkaline with 50% potassium hydroxide and the ether which separated was extracted with benzene. The benzene extract was dried over potassium hydroxide, the benzene removed in vacuo and the residue distilled. B. p. 118-119°/0.25 mm, yield 1.11 g (50%). Yellow viscous liquid soluble in organic solvents and water, $n^{18}D$ 1.4812.

Found %: C 68.12; H 10.59; N 9.91. $C_{16}H_{30}O_2N_2$. Calculated %: C 68.09; H 10.63; N 9.93.

7-Dimethylaminomethyl-6-(β-benzoyloxyethyl)-1-azabicyclo-(3.2.1)-octane (VIc). From 2 g of the amino alcohol (Vb) and 1.5 g of benzoyl chloride there was obtained, by the method described for compound (VIa), 1.8 g (60.5%) of the ether (VIc) as a colorless somewhat viscous oil, soluble in organic solvents. B. p. 181-183°/0.4 mm.

Found %: C 71.94, 72.14; H 8.57, 8.67. $C_{19}H_{28}O_2N_2$. Calculated %: C 72.12; H 8.85.

7-Dimethylaminomethyl-6-(β-acetoxyethyl)-1-azabicyclo-(3.2.1)-octane (VId). To a solution of 2.2 g of the amino alcohol (Vb) in 20 ml of benzene was added 0.9 g of acetyl chloride. The mixture was refluxed for 2½ hours and subsequently treated by the method described for compound (VIb). There was obtained 2 g (76%) of compound (VId) in the form of a mobile colorless oil, b. p. 111-115°/0.3 mm, $n^{18}D$ 1.4871.

Found %: C 65.85; H 10.16; N 10.94. $C_{14}H_{26}O_2N_2$. Calculated %: C 66.14; H 10.23; N 11.02.

7-Dimethylaminomethyl-6-(β-propionyloxyethyl)-1-azabicyclo-(3.2.1)-octane (VIe). To a solution of 2.2 g of the amino alcohol (Vb) in 30 ml of benzene was added 1.5 g of propionyl chloride. After refluxing for two hours the reaction mixture was treated in the usual way and there was obtained 1.5 g (54%) of compound (VIe). B. p. 130°/0.4 mm, $n^{16}D$ 1.483. Yellow mobile liquid, soluble in water and organic solvents.

The dipicrate was obtained as yellow crystals soluble in alcohol and acetone, and insoluble in ether and water.

Found %: C 44.55; H 4.68. $C_{27}H_{34}O_{16}N_8$. Calculated %: C 44.50; H 4.68.

7-Aminomethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane (VII). Method A. To a solution of 0.25 g of the amino alcohol (Vf) in 10 ml of benzene was added, with cooling and stirring, 10 ml to thionyl chloride. The reaction mixture was heated at 70° for two hours after which it was evaporated in vacuo and treated with 50% potassium hydroxide. The amino chloride (VII) which separated was extracted with ether. The ether extract was dried over potassium hydroxide, filtered, and the filtrate treated with 6% alcoholic solution of picric acid. The dipicrate of (VII) separated as yellow crystals, soluble in acetone, difficultly soluble in alcohol, and insoluble in water and ether. M. p. 208° (from water-acetone mixture).

Found %: C 39.94; H 3.98; N 17.11; Cl 5.29. $C_{22}H_{25}O_{14}N_8Cl$. Calculated %: C 39.99; H 3.78; N 16.96; Cl 5.37.

Method B. A mixture of 2 g (0.009 mole) of 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane and 3.33 (0.018 mole) of potassium phthalimide in 30 ml of absolute alcohol was refluxed for 30 hours. At the end of this period the potassium chloride which separated was filtered off and the alcoholic solution evaporated in vacuo and the residue dissolved in 20 ml of hydrochloric acid (1:1). This solution was refluxed for 16 hours and the hydrochloric acid removed in vacuo. The dihydrochloride of (VII) thus formed was treated with 40% sodium hydroxide solution and the free base which separated was extracted with ether. The ethereal solution was treated to yield the dipicrate, m. p. 208° (from water-acetone mixture). The latter does not depress the melting point in mixture with the dipicrate obtained by method A.

Found %: C 40.24; H 4.10; N 16.87, 16.99; Cl 5.68, 5.37. $C_{22}H_{25}O_{14}N_8Cl$. Calculated %: C 39.99; H 3.78; N 16.96; Cl 5.37.

SUMMARY

Hydrolysis of the ethyl ester of6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid gives 6-carbethoxymethyl-1-azabicyclo-(3.2.1)-octan-7-carboxylic acid. Starting from the latter acid a number of 7-alkyl-(aryl)-aminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes have been synthesized.

Certain esters of 7-dialkylaminomethyl-6-(β-hydroxyethyl)-1-azabicyclo-(3.2.1)-octanes have also been prepared.

An explanation has been given for the difference in the lability of the chlorine atom in positions 6 and 7 in 7-chloromethyl-6-(β-chloroethyl)-1-azabicyclo-(3.2.1)-octane.

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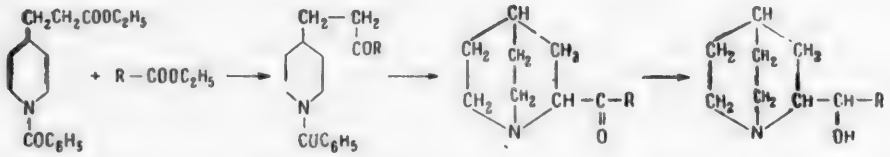
* Original Russian pagination. See C. B. Translation.

SYNTHESIS OF SUBSTITUTED QUINUCLIDINE-2-CARBINOLS

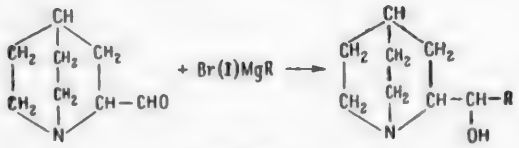
L. N. Iakhontov, S. V. Iatsenko and M. V. Rubtsov

The synthesis of substituted quinuclidine-2-carbinols – compounds of the quinine alkaloid type – was first accomplished by P. Raabe in 1911 [1]. The Raabe method consists in condensing the ethyl esters of β-[N-benzoyl-piperidyl-(4)]-propionic acid and of some other acid (for example, cinchoninic or quininic acids) followed by closure of the quinuclidine ring and reduction of the resultant ketone to the corresponding substituted quinuclidine-2-carbinol.



Up to the present this was the only method for the preparation of substituted quinuclidine-2-carbinols. By this method were obtained quinine [2], hydroquinone [3] as well as a number of analogs and isomers of quinine alkaloids [4-6].

The present paper describes a new method of preparation of substituted quinuclidine-2-carbinols according to the following scheme



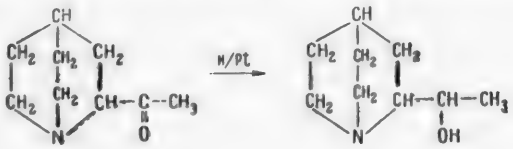
(I) R = CH_3

(II) R = C_2H_5

(III) R = 

The starting material is 2-formylquinuclidine [7] which on interacting with various organomagnesium compounds gives rise to the formation of the corresponding substituted quinuclidine-2-carbinols. In this way we have prepared (quinuclidine-2)-methyl carbinol (I), (quinuclidine-2)-ethyl carbinol (II) and (quinuclidine-2)-(naphthyl-1)-carbinol (III).

(Quinuclidine-2)-methyl carbinol was also prepared by reducing 2-acetylquinuclidine [8] (IV) in the presence of platinum catalyst.



(IV) (I)

Now, reduction of compound (IV) in absolute alcohol as the solvent gives, as is also the case in the organomagnesium method, a mixture of two diastereoisomeric (quinuclidine-2)-methyl carbinols, a crystalline one and another in the form of an oil. Reduction of compound (IV) in distilled water gives only the crystalline diastereoisomer.

EXPERIMENTAL

(Quinuclidine-2)-Methyl Carbinol (I)

1) From 2-formylquinuclidine. To the Grignard reagent, prepared from 1.34 g of methyl iodide and 0.23 g of magnesium in anhydrous ether, was added at 0° a solution of 1.3 g of freshly prepared 2-formylquinuclidine in 10 ml of anhydrous ether. The reaction mixture was stirred at room temperature for 10 hours after which it was treated with 25 ml of 5% hydrochloric acid and extracted with ether. The hydrochloric acid solution was made alkaline with excess of 50% potassium hydroxide and the base which separated was extracted with ether. The ether extract was dried over potassium hydroxide, the ether removed and the residue distilled in vacuo. Yield 1.04 g (74.5%) of a mixture of the diastereoisomeric racemates of quinuclidine-2-methyl carbinol in the form of a colorless oil, b. p. 60° (2 mm). The substance dissolves easily in the usual organic solvents and in water; $n^{20}D$ 1.4913.

Found %: N 9.09. $C_9H_{17}ON$. Calculated %: N 9.03.

The hydrochloride was obtained as a colorless oil by treating an ethereal solution of the base with an alcoholic solution of hydrogen chloride.

The picrate forms yellow crystals melting at 173-175°.

Found %: C 46.71, 47.05; H 5.08, 5.24; N 14.71. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: C 46.87; H 5.21; N 14.58.

In order to resolve the diastereoisomerides use was made of the difference in the solubilities of their hydrochlorides in alcohol and acetone.

0.77 g of the base (I) was mixed with 2 ml of 10% alcoholic hydrogen chloride and 10 ml of anhydrous acetone. The white crystalline precipitate which separated was filtered off and recrystallized from absolute alcohol. There was obtained 0.27 g of (quinuclidine-2)-methyl carbinol hydrochloride (racemate A). Colorless crystals, easily soluble in water, sparingly soluble in the usual organic solvents; m. p. 218-220°.

Found %: C 56.12, 55.94; H 9.41, 9.28; N 7.24, 7.03. $C_9H_{17}ON \cdot HCl$. Calculated %: C 56.39; H 9.40; N 7.31.

The free base is a colorless oil boiling at 92-95° (3 mm), $n^{20}D$ 1.5040. On standing the oil crystallizes to colorless crystals, m. p. 38°. The substance is easily soluble in water and in organic solvents.

Found %: N 8.90. $C_9H_{17}ON$. Calculated %: N 9.03.

The picrate forms yellow crystals, soluble in acetone, insoluble in alcohol and ether; m. p. 163-165°.

Found %: C 46.71, 47.05; H 5.08, 5.24; N 14.71. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: C 46.87; H 5.21; N 14.58.

The acetone-alcoholic mother-liquor obtained after separating racemate A was evaporated in vacuo. The residue was triturated with 3 ml of anhydrous acetone. The deliquescent crystals which separated were recrystallized from absolute alcohol. After two crystallizations another 0.03 g of the hydrochloride of racemate A was obtained, m. p. 218-220°.

The acetone mother liquor was evaporated in vacuo, yielding 0.2 g of the hydrochloride of (I) (racemate B) as a colorless oil which is easily soluble in water and alcohol, difficultly soluble in acetone, and insoluble in ether.

The free base is a colorless oil easily soluble in water and organic solvents, b. p. 60° (2 mm), $n^{20}D$ 1.4871.

Found %: N 8.92. $C_9H_{17}ON$. Calculated %: N 9.03.

The picrate is formed as yellow crystals, soluble in acetone, insoluble in alcohol and ether; m. p. 183-185°.

Found %: N 14.63. $C_9H_{17}ON \cdot C_6H_3O_7N_3$. Calculated %: N 14.58.

2) From 2-acetylquinuclidine. (a) 1 g of 2-acetylquinuclidine in 20 ml of absolute alcohol was hydrogenated at 18-20° and at a pressure of 20-25 cm water gauge, in the presence of 0.1 g of platinum catalyst prepared by Adams' method. Hydrogenation was completed in three hours. The catalyst was filtered off, the filtrate evaporated and the residue distilled in vacuo. There was obtained 0.91 g (89.7%) of a mixture of the diastereoisomeric (quinuclidine-2)-methyl carbinols in the form of a colorless oil boiling at 60° (2 mm). The substance dissolves easily in organic solvents and water; $n^{20}D$ 1.4913.

The hydrochloride is formed as a colorless oil. The picrate forms yellow crystals, m. p. 173-175°.

The mixture of the diastereoisomerides was resolved into the racemates A and B by the method described above.

(b) 2.8 g of 2-acetylquinuclidine dissolved in 28 ml of distilled water was hydrogenated at a temperature of 18-20° and a pressure of 20-25 cm water gauge, in the presence of 0.3 g of platinum catalyst prepared by Adams' method. Hydrogenation was completed in three hours. The catalyst was filtered off, the filtrate evaporated in vacuo and traces of moisture removed by steam distillation with benzene. The residue was dissolved in anhydrous ether, a small amount of fluffy precipitate which formed was filtered off, the ether removed and the residue distilled in vacuo. There was obtained 2.05 g (72.5%) of racemate A of (quinuclidine-2)-methyl carbinol. Colorless oil, b. p. 92-95° (3 mm), $n^{20}D$ 1.5040. On standing the substance crystallized in the form of white crystals melting at 38°.

The hydrochloride forms colorless crystals, m. p. 218-220°. The picrate is formed as yellow crystals, m. p. 163-165°.

(Quinuclidine-2)-ethyl carbinol (II) was prepared by the method using the Grignard reagent in a manner similar to that employed in the preparation of (quinuclidine-2)-methyl carbinol. From 1.3 g of freshly prepared 2-formylquinuclidine, 1.4 g of ethyl bromide and 0.32 g of magnesium there was obtained 0.8 g (50.9%) of a mixture of the diastereoisomeric racemates of (II). Colorless oil, b. p. 100-110° (45 mm). The substance is easily soluble in water and organic solvents; $n^{20}D$ 1.4883.

Found %: N 8.14. $C_{10}H_{19}ON$. Calculated %: N 8.28.

The hydrochloride is an oil. The picrate is formed as yellow crystals melting at 149-150° from a mixture of alcohol and ether.

Found %: C 48.10; H 5.76; N 14.04, 14.18. $C_{10}H_{19}ON \cdot C_6H_3O_7N_3$. Calculated %: C 48.29; H 5.54; N 14.07.

(Quinuclidine-2)-(naphthyl-1)-carbinol (III). To 0.26 g of magnesium turnings activated by heating with a few crystals of iodine, was added a solution of 2.23 g of α-bromonaphthalene in 10 ml of anhydrous ether over a period of 45 minutes. The reaction mixture was refluxed for 4 hours. To the naphthyl magnesium bromide so obtained was added, at 0°, a solution of 1.6 g of freshly prepared 2-formylquinuclidine in 2 ml of anhydrous ether. The reaction mixture was stirred for 14 hours at room temperature, after which it was treated with 50 ml of 5% hydrochloric acid. Nonbasic constituents of the mixture were separated by extraction with ether. The hydrochloric acid solution was then made alkaline with 50% potassium hydroxide, the base which separated was extracted several times with ether and the extract, after drying over potassium hydroxide, was evaporated to a volume of 25 ml. After standing for two days there crystallized 0.1 g of a substance which was recrystallized from anhydrous acetone as colorless needles, m. p. 200-201°. The substance dissolves in alcohol and acetone, is difficultly soluble in ether and insoluble in water.

The hydrochloride forms colorless crystals melting at 203.5-205.5°. It is easily soluble in water, alcohol, chloroform and acetone, and insoluble in ether.

The base and its hydrochloride are identical, respectively, with the base and the hydrochloride of racemate A of (quinuclidine-2)-(naphthyl-1) -carbinol prepared earlier by Raabe's method from β-[N-benzoylpiperidyl-(4)]-propionic acid and α-naphthoic acid [5].

The ethereal mother liquor left after separation of racemate A was evaporated in vacuo. The residue was

distilled at a pressure of 0.4 mm. Two fractions were collected: fraction 1 (0.8 g), boiling at 60-80° was identified as unreacted 2-formylquinuclidine, fraction No. 2 (0.45 g) boiling at 192-195°, constituted a mixture of the diastereoisomers of (III) in the form of a viscous oil. In order to resolve the diastereoisomerides the oil was triturated with anhydrous ether. The crystalline product which separated (0.18 g) melted at 200-201° after recrystallization from anhydrous acetone and did not give melting point depression in mixture with racemate A of (III).

The ethereal solution obtained after separating racemate A was evaporated in vacuo. The residue (0.23 g) crystallized on standing in the dessicator over caustic potash. For the purpose of further purification the compound was transformed into its hydrochloride. This was triturated with anhydrous acetone. There were obtained colorless crystals melting at 275° (decomp.). The free base liberated from the hydrochloride was in the form of an oil which crystallized on standing in a vacuum-dessicator over potassium hydroxide. The crystals melt at 64-67°*. The substance dissolves easily in alcohol, acetone, chloroform and ether.

The hydrochloride forms colorless crystals melting at 289-290°* (after two recrystallizations from alcohol). It is soluble in water, alcohol, chloroform; insoluble in acetone and ether.

Found %: C 70.72; H 7.40. $C_{18}H_{21}ON \cdot HCl$. Calculated %: C 71.14; H 7.30.

The compounds thus synthesized are, respectively, the free base, (quinuclidine-2)-(naphthyl-1)-carbinol (racemate B), and its hydrochloride, both of which have been prepared earlier [5] by Raabe's method from the ethyl esters of β-[N-benzoylpiperidyl-(4)]-propionic and α-naphthoic acids.

The combined yield of racemates A and B of (III) was 35.3% (based on the 2-formylquinuclidine).

SUMMARY

1. A new method for the synthesis of substituted quinuclidine-2-carbinols from 2-formylquinuclidine and organomagnesium compounds has been described.

2. (Quinuclidine-2)-methyl carbinol, (quinuclidine-2)-ethyl carbinol and (quinuclidine-2) (naphthyl-1)-carbinol have been synthesized by the method outlined.

3. (Quinuclidine-2)-methyl carbinol has also been prepared by reduction of 2-acetylquinuclidine in the presence of a platinum catalyst. In this case a mixture of the two diastereoisomerides has been obtained when reduction was effected in absolute alcohol, just as is the case in the synthesis using the Grignard reagents; reduction in water, however, gave rise to the formation of only one of the two diastereoisomerides.

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[7] M. V. Rubtsov and L. N. Iakhontov, Ibid. 25, 2143, (1955).**

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* In the paper [5] it was indicated that racemate B of (quinuclidine-2)-(naphthyl-1)-carbinol melts at 63-65° and its hydrochloride at 267.5-269°.

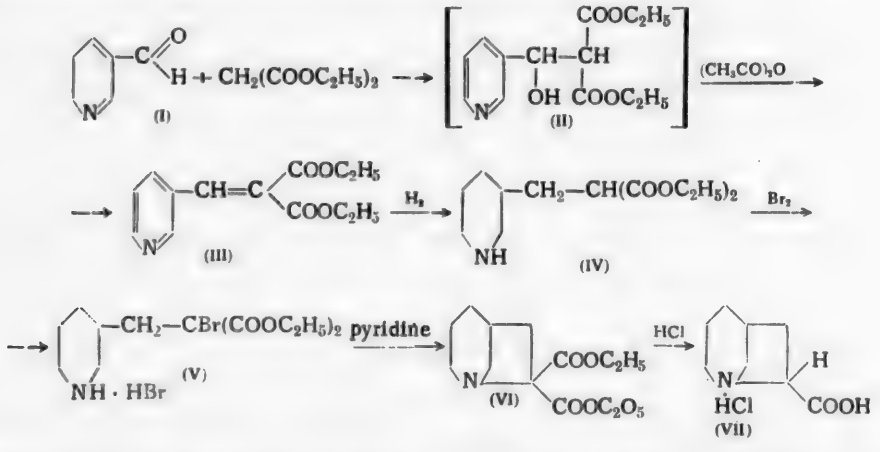
** Original Russian pagination. See C. B. Translation.

THE SYNTHESIS OF 1-AZABICYCLO-[3.2.1]-OCTANE-7-CARBOXYLIC ACID

A. K. Chizhov and M. V. Rubtsov

The information in the literature on 1-azabicyclo-[3.2.1]-octanes is limited to the description of the synthesis of the unsubstituted bicyclic compound [1] and some of its 6-substituted derivatives [2,3]. Definite interest is offered by the synthesis of the unknown 1-azabicyclo-[3.2.1]-octanes with substituents in the 7 position, inasmuch as the latter are isomeric with the 2-substituted derivatives of quinuclidine (1-azabicyclo-[2.2.2]-octane), to which the quinine alkaloids and a number of other compounds obtained in recent years are related. Among these compounds are found substances with valuable biological properties.

The present work is devoted to the synthesis of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid, which in turn can serve as the starting material for the preparation of 7-substituted derivatives of 1-azabicyclo-[3.2.1]-octane. The synthesis of the acid was accomplished by the following scheme



Nicotinic aldehyde (I) was condensed with malonic ester in the presence of piperidine at room temperature; in this way the diethyl ester of 2-(pyridyl-3')-2-hydroxyethane-1,1-dicarboxylic acid (II) was produced. Heating of the diester (II) with acetic anhydride resulted in the splitting out of a molecule of water and the formation of the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid (III). The hydrochloride of the diester (III) was further subjected to reduction in alcohol solution in the presence of platinic oxide (according to Adams' method), whereupon the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid (IV) was obtained. For the subsequent transition from the 3-substituted piperidine to the azabicyclic system, compound (IV) was treated with bromine in chloroform solution. The diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid (V) which was formed was converted by heating with pyridine to 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane (VI). Boiling the diester (VI) with concentrated hydrochloric acid led to the formation of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid (VII).

EXPERIMENTAL

Diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid (III). 17.0 g. of nicotinic aldehyde, 181.3 g

of malonic ester, and 1.5 g of piperidine were allowed to stand at 20° for 7 days. The unreacted malonic ester and piperidine were distilled off in vacuo. To the residue, which consisted of the diethyl ester of 2-(pyridyl-3')-2-hydroxyethane-1,1-dicarboxylic acid was added 94.2 g of acetic anhydride and the mixture was heated for 2 hours at 115-117°. Then the acetic anhydride and acetic acid were distilled off in vacuo, and the remaining material was distilled at 0.25 mm and the fraction was collected that boiled within the limits 130-136°. Yield of diethyl ester (III) 30.6 g (77.5%), $n^{20}D$ 1.5275. Colorless liquid, soluble in ether, insoluble in water.

Found %: C 62.01; H 6.28. $C_{13}H_{15}O_4N$. Calculated %: C 62.63; H 6.06.

Hydrochloride – white, crystalline powder with m. p. 152-153°. Readily soluble in water and alcohol.

Diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid (IV). To a solution of 11.58 g of the hydrochloride of the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid in 130 ml of anhydrous alcohol was added 0.51 g of platinic oxide prepared according to the method of Adams. The reaction mixture was shaken with hydrogen at room temperature. The hydrogenation was completed in 10 hours. The platinum black was filtered off and the alcoholic solution was evaporated in vacuo at 40°. The hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid was obtained as an extremely hygroscopic, viscous, caramel-like mass, readily soluble in chloroform. Quantitative yield.

To isolate the base, 8.18 g of the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid was treated with 20 ml of 50% aqueous potassium carbonate solution. The oil that separated was extracted with ether, the extract was dried with potassium carbonate, the ether was distilled off in vacuo, and the residue was subjected to vacuum distillation. Yield of diethyl ester (IV) 4.54 g (63.5%).

B. p. 125-126° (0.3 mm), $n^{20}D$ 1.4638, d^{20}_4 1.0599, MR_D 66.41; calculated 66.94.

Found %: N 5.38, 5.56. $C_{13}H_{21}O_4N$. Calculated %: N 5.46.

7,7-Dicarboethoxy-1-azabicyclo-[3.2.1]-octane (VI). To a solution of 12.13 g of the hydrochloride of the diethyl ester of 2-(piperidyl-3')-ethane-1,1-dicarboxylic acid in 36 ml of dry chloroform was added over a period of 12 hours a solution of 8.8 g of bromine in 101 ml of dry chloroform at room temperature. The mixture was stirred for 2 hours longer, after which the chloroform was distilled off in vacuo at 35-40°. To the oily residue was added 5 times its volume of absolute ether. After trituration and 4 hours' standing at room temperature the oil crystallized. The crystals were filtered off, washed with ether, and dried in the air. Yield of hydrobromide of the diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid 17.8 g. The compound formed yellowish crystals, readily soluble in water, difficultly soluble in ether. M. p. 90-92°.

12.53 g of the hydrobromide of the diethyl ester of 2-(piperidyl-3')-1-bromoethane-1,1-dicarboxylic acid was suspended in 12 ml of water and 12 ml of 50% aqueous potassium carbonate solution was added. The base that separated was extracted with ether, the ethereal extract was evaporated in vacuo, and the residue was dissolved in 51 ml of dry pyridine. The pyridine solution was heated to boiling for 2 hours. Then the pyridine was evaporated in vacuo. To the residue was added 8.3 ml of 50% aqueous potassium carbonate solution and the resulting mixture was extracted with ether. The ethereal extract was dried with potassium carbonate, the ether was distilled off, and the remaining material was distilled in vacuo. A fraction was collected that boiled at 152-154° (5 mm). Yield 4.44 g (57.8%). It should be noted that the fraction that distilled below 152° had the same refractive index and upon hydrolysis with hydrochloric acid yielded the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid.

$n^{20}D$ 1.4770, d^{20}_4 1.1104, MR_D 64.97; calculated 65.08.

Found %: C 61.28; H 8.12. $C_{13}H_{21}O_4N$. Calculated %: C 61.15; H 8.28

Hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid (VII). 3.4 g of 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane and 35 ml of concentrated hydrochloric acid were refluxed for 8 hours. The hydrochloric acid solution was evaporated on a steam bath until crystallization began. The residue was cooled to room temperature and after standing for an hour and a half the crystals that were obtained were diluted with acetone and filtered. 2.41 g (94.5%) of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid was obtained. M. p. 273-274°. After recrystallization from a mixture of alcohol and ether, m. p. 290-293°.

Found %: C 50.40; H 7.41; N 7.38, 7.26; Cl 18.63. $C_8H_{13}O_2N \cdot HCl$. Calculated %: C 50.15; H 7.37; N 7.31; Cl 18.51.

SUMMARY

The synthesis of the hydrochloride of 1-azabicyclo-[3.2.1]-octane-7-carboxylic acid has been carried out, starting from nicotinic aldehyde through the diethyl ester of 2-(pyridyl-3')-vinyl-1,1-dicarboxylic acid, the diethyl ester of 2-(piperidyl-3') ethane-1,1-dicarboxylic acid, and 7,7-dicarboethoxy-1-azabicyclo-[3.2.1]-octane.

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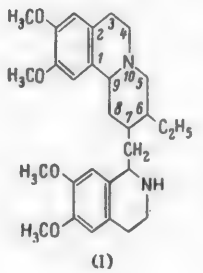
INVESTIGATIONS IN THE ISOQUINOLINE SERIES

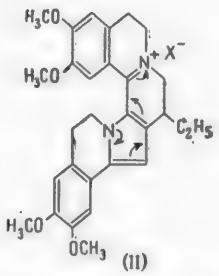
XII. SYNTHESIS OF 4',5'-DIMETHOXY-5,6-DIMETHYL-7-(1''-METHYL-6'',7''-DIMETHOXY-1'',2'',3'',4''-TETRAHYDROISOQUINOLYL)-3,4,5,6,7,8-HEXAHYDROBENZO[1',2':1,2]QUINOLIZINE

R. P. Evstigneeva, N. M. Kashnikova, M. S. Bainova and N. A. Preobrazhenskii

One of the interesting properties of the alkaloid emetine (I) is its ability to be converted by the action of mild oxidizing agents to a red compound, so-called rubremetine [1-3]. The structure of the latter has not been established up to the present time, although several ideas have been expressed concerning this problem [4-8].



(I)



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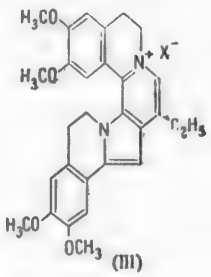
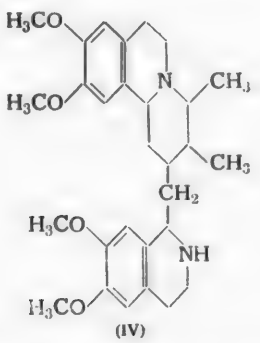


(III)

The most probable of the formulas proposed for rubremetine, (II) and (III) [6,8], assume the formation of a new ring system with the participation of the carbon atom C_8. The formation of such a system obviously would be difficult in the presence of substituents on that carbon. In order to more fully investigate the effect of substituents in the ring on the formation of rubremetine, we have undertaken the synthesis of two analogs of emetine that have alkyl substituents in the two free positions on carbons C_5 and C_8: 1) 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]quinolizine (IV) and 2) 8-methylemetine (V).



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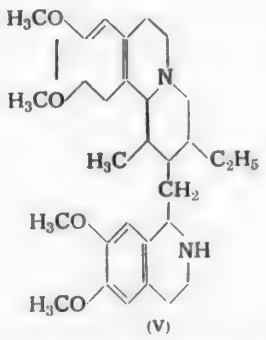
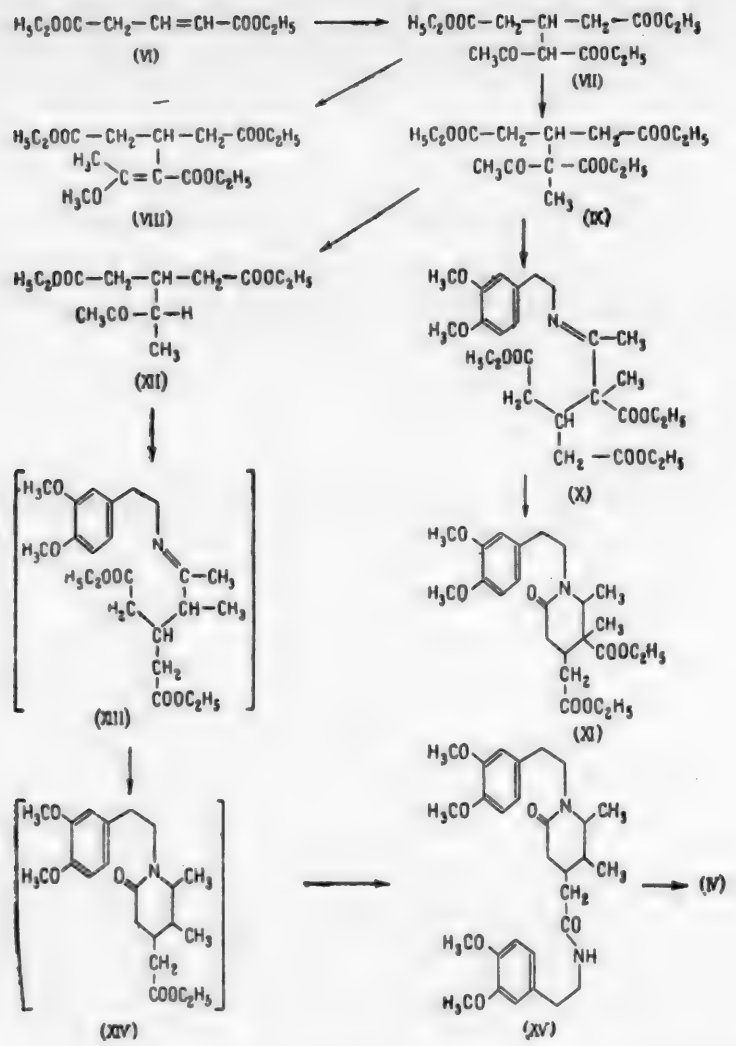


(V)

The synthesis of the first of these compounds is the subject of this communication. Compound (IV) is interesting also because it corresponds to one of the structures proposed for emetine.

The synthesis was based on a scheme developed for emetine [9].



The ethyl ester of glutaconic acid (VI) was condensed with ethyl aceto-acetate in the presence of sodium ethylate. In this way the ethyl ester of β-(acetocarbethoxy)-methylglutaric acid (VII) was obtained.

By its further methylation with methyl iodide in the presence of sodium alcoholate, the ethyl ester of β-(α'-aceto-α'-carboethoxy)-ethylglutaric acid (IX) was obtained. The reaction usually proceeded over a period of 1 hour, and with more prolonged heating the ortho-methylated product (VIII) also was obtained. The ethyl ester of β-(α'-aceto-α'-carboethoxy)-ethylglutaric acid yielded a Schiff base (X) with homoveratryl-amine. After hydrogenation in the presence of a platinum catalyst and heating in vacuo it was converted to the ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-α-carboethoxy-α-piperidone-γ-acetic acid (XI).

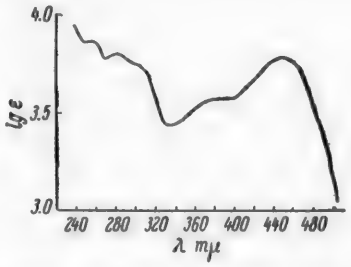
The tricarboxylic ester (IX) was subjected to selective saponification with the calculated amount of sodium alcoholate and water, and after acidification and decarboxylation the ethyl ester of β-(α'-aceto)ethylglutaric acid (XII) was obtained. All attempts to increase the yield by changing the conditions were futile.

The ethyl ester of β-(α'-aceto)ethylglutaric acid was condensed successively with two molecules of homoveratrylamine without separating the intermediate products. The first molecule of homoveratrylamine

reacted under the usual conditions when the reagents were mixed. The Schiff base (XIII) that was produced was hydrogenated in the presence of platinum catalyst, and the reduction product was cyclicized to the corresponding piperidone (XIV) by heating on a boiling water bath in vacuo. The latter compound was condensed with the second molecule of homoveratrylamine by heating to 180° for 1 hour. The diamide (XV) was isolated as a thick yellow oil.

After cyclization with phosphorus oxychloride and reduction of the chloride, 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2] quinolizine (IV) was obtained as a thick, light yellow oil. The hydrochloride of compound (IV) was isolated in an amorphous condition. The base 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]quinolizine was oxidized with bromine. An orange-red substance separated, which was similar to rubremetine in physicochemical properties and absorption spectrum (Fig. 1).

Thus, the presence of an alkyl substituent on carbon atom C_8 did not prevent the formation of a rubro-compound.



Ultraviolet absorption spectrum in alcohol of the product of oxidation of compound (IV) with bromine.

EXPERIMENTAL

Ethyl ester of β-(acetocarboethoxy)methylglutaric acid (VII). To a mixture consisting of 21 g of ethyl glutaconate, 29.6 g of freshly distilled acetoacetic ester, and 20 ml of anhydrous ethyl alcohol there was added, with heating, 1/6 part every 2 hours of a solution of sodium ethylate prepared from 1.5 g of sodium and 20 ml of anhydrous ethyl alcohol. Heating was continued for 12 hours. When the reaction was ended, the alcohol was distilled off in vacuo, and 30 ml of ice water was added to the residue. The oil that separated was extracted with 100 ml of ether. After the extract had been dried with sodium sulfate, the solvent was distilled off and the residue was distilled. Yield 22.6 g (63.3%). The ethyl ester of β-(acetocarboethoxy) methylglutaric acid was a colorless liquid, soluble in alcohol, ether, and benzene, insoluble in water.

B. p. 167-169° (2.5-3 mm), d^{20}_4 1.1007, $n^{20}D$ 1.4500, MR_D 77.27; calculated 76.44 (for the keto form), 77.49 (for the enol form).

Found %: C 56.89, 57.12; H 7.33, 7.58; $C_{15}H_{24}O_7$. Calculated %: C 56.93; H 7.65.

Ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid (IX). To a solution of sodium ethylate prepared from 1.43 g of sodium and 29 ml of anhydrous ethyl alcohol were added 16 g of the ethyl ester of β-(acetocarboethoxy)methylglutaric acid and 21.3 g of methyl iodide. The reaction mass was heated to boiling for 1 hour. The alcohol was distilled off in vacuo, and 30 ml of water was added to the residue. The oil that separated was extracted with ether. The extract was dried with sodium sulfate. After the solvent was distilled off, the residue was distilled. Yield 11.6 g (69.4%). The ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid was a colorless liquid, soluble in organic solvents, insoluble in water.

B. p. 149-151° (1.4 mm), d^{20}_4 1.1108, $n^{20}D$ 1.4591, MR_D 81.13; calculated 81.06.

Found %: C 58.29, 57.92; H 7.66, 7.95. $C_{16}H_{26}O_7$. Calculated %: C 58.14; H 7.94.

Upon more prolonged heating of the reaction mass (2.5-3 hours) the ortho-methylated product (VIII) also was obtained in considerable amounts.

B. p. 159-160° (1.5 mm), d^{20}_4 1.1084, $n^{20}D$ 1.4638, MR_D 82.22; calculated 82.22.

Found %: C 58.41, 58.15; H 7.98, 7.69. $C_{16}H_{26}O_7$. Calculated %: C 58.14; H 7.94.

Ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-δ-carboethoxy-α-piperidone-γ-acetic acid (XI). 5 g of the ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid was mixed with 8.25 g of β-(3,4-dimethoxyphenyl)ethylamine. The next day the reaction mass was heated to 70° for 30 minutes. Upon cooling, it was dissolved in 25 ml of anhydrous ethyl alcohol, glacial acetic acid was added until there was a

neutral reaction, and the mixture was hydrogenated in the presence of 0.3 g of platinic oxide at 30 atm for 4 hours. The catalyst was filtered off, the alcohol was distilled off, and the residue was heated in vacuo on a boiling water bath for 1 hour. Upon cooling, the reaction mass was dissolved in ether and washed with 5% hydrochloric acid solution, then with sodium bicarbonate solution. The extract was dried with sodium sulfate. The solvent was distilled off and the residue was distilled. Yield 24 g (35.4%). The ethyl ester of N-[β'-(3,4-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-δ-carboethoxy-α-piperidone-γ-acetic acid was a thick, oily liquid with a yellow color, readily soluble in organic solvents. B. p. 208-210° (0.3 mm).

Found %: C 64.36, 64.29; H 7.86, 8.07; N 3.33, 3.30. $C_{24}H_{35}O_7N$. Calculated %: C 64.12; H 7.85; N 3.11.

The Schiff base (X) separated in the crystalline condition on prolonged standing. After recrystallization from anhydrous ethyl alcohol it melted at 88-89°.

Found %: C 63.49; H 7.72; N 3.01. $C_{26}H_{39}O_8N$. Calculated %: C 63.25; H 7.97; N 2.84.

Ethyl ester of β-(α'-aceto)ethylglutaric acid (XII). To a solution of sodium alcoholate prepared from 1.9 g of sodium and 36.5 ml of anhydrous ethyl alcohol were added 25.2 g of the ethyl ester of β-(α'-aceto-α'-carboethoxy)ethylglutaric acid and 1.41 g of water. The mixture was kept at room temperature for 12 hours and then heated to boiling for 1 hour. Upon cooling of the mixture, the excess alcohol was distilled off in vacuo and 18 ml of water was added to the residue. The solution was shaken with ether to remove the unsaponified material, and the aqueous layer was acidified with hydrochloric acid and extracted with ether. After being dried with sodium sulfate, the solvent was distilled off and the residue was heated in vacuo in a current of nitrogen at 170-180° for 40 minutes. Upon cooling, the reaction mass was dissolved in 40 ml of benzene and washed with sodium bicarbonate. The benzene was distilled off and the residue was distilled. Yield 0.6 g (3%). The ethyl ester of β-(α'-aceto)ethylglutaric acid was a colorless liquid, soluble in organic solvents, insoluble in water. B. p. 110-112° (1.1 mm).

Found %: C 60.80, 60.33; H 8.25, 8.37. $C_{13}H_{22}O_5$. Calculated %: C 60.42; H 8.58.

β''-(3'',4''-Dimethoxyphenyl)ethylamide-N-[β-(3',4'-dimethoxyphenyl)-ethyl]-δ,ε-dimethyl-α-piperidone-γ-acetic acid (XV). 0.55 g of the ethyl ester of β-(α'-aceto)ethylglutaric acid was mixed with 0.38 g of β-(3,4-dimethoxyphenyl)ethylamine; thereupon evolution of heat was observed. The mixture was left at room temperature overnight. Then 10 ml of anhydrous ethyl alcohol was added to the reaction mass and it was hydrogenated in the presence of 0.2 g of platinic oxide at a hydrogen pressure of 0.5 atm. The excess alcohol was distilled off and the residue was heated on a boiling water bath in vacuo for 1 hour. The piperidone derivative formed was not isolated but was heated with 0.43 g of β-(3,4-dimethoxyphenyl)ethylamine at 180° for 1 hour. Upon cooling, the reaction mass was carefully washed with dry ether and dried in a dessicator. Yield 0.9 g (82%). The diamide (XV) was a thick yellow oil, readily soluble in alcohol, difficultly soluble in toluene, insoluble in ether and water.

Found %: N 5.81, 5.51. $C_{29}H_{40}O_6N_2$. Calculated %: N 5.46.

Hydrochloride of 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-[1',2';1,2]quinolizine (IV). A solution of 0.9 g of β''-(3'',4''-dimethoxyphenyl)ethylamido-N-[β-(3',4'-dimethoxyphenyl)ethyl]-δ,ε-dimethyl-α-piperidone-γ-acetic acid in 5 ml of toluene and 7 ml of phosphorus oxychloride was heated to gentle boiling for 1 hour. Upon cooling, the excess oxychloride and toluene was distilled off in vacuo. The residue was dissolved in 13 ml of 6% hydrochloric acid. The solution was evaporated to dryness in vacuo. The remaining thick, dark yellow oil was dissolved in anhydrous ethyl alcohol and treated with an alcoholic solution of ammonia. A precipitate of inorganic salts was filtered off. The alcoholic solution was placed in an autoclave and hydrogenated in the presence of 2 g of Raney nickel catalyst at 110 atm and 75-80° for 1.5 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in 8 ml of water and treated, while cooling, with 5% sodium hydroxide solution. The oil that separated was extracted with ether. After being dried with potassium carbonate, the ether was distilled off. The residue was a light yellow oil (0.5 g). The hydrochloride was obtained from the ether solution of the base by treating it with ether saturated with dry hydrogen chloride. It was a colorless, amorphous substance, readily soluble in alcohol and water, insoluble in ether. M. p. 134-135° (it deformed at 112-116°).

Found % N 4.72, 4.74. $C_{29}H_{40}O_4N_2 \cdot 2HCl$. Calculated % N 4.79.

Oxidation of compound (IV) with bromine. To a solution of 0.1 g of the base 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo[1',2':1,2]-quinolizine in 0.3 ml of chloroform was gradually added a solution of 0.04 ml of bromine in 1.5 ml of chloroform. In 10 minutes, the mixture was treated with ammonia solution until a turbidity appeared. The chloroform solution was dried with potassium carbonate. After the solvent was distilled off, the compound was extracted with hot water. The extract was evaporated to dryness. The residue was dissolved in anhydrous alcohol. When absolute ether was added, an orange-red precipitate separated out. After repeated reprecipitation of the material from alcohol the m. p. was 164-180° (it deformed at 160°).

λ_{max} 286 mμ, lg ε (3.80); 445-455 mμ, lg ε (3.78); λ_{min} 270 mμ, lg ε (3.78); 340 mμ, lg ε (3.44).

Found % N 5.09, 4.61. $C_{29}H_{33}O_4N_2Br$. Calculated % N 5.06.

SUMMARY

1. The synthesis of 4',5'-dimethoxy-5,6-dimethyl-7-(1''-methyl-6'',7''-dimethoxy-1'',2'',3'',4''-tetrahydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-[1',2':1,2]quinolizine, an analog of emetine, has been carried out.

2. The rubro-compound has been obtained by oxidation of the emetine analog with bromine, and in this way it has been shown that a substituent on carbon atom C_5 does not prevent formation of the rubremetine analog.

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INVESTIGATIONS IN THE ISOQUINOLINE SERIES

XIII. SYNTHESIS OF 8-METHYLEMETINE

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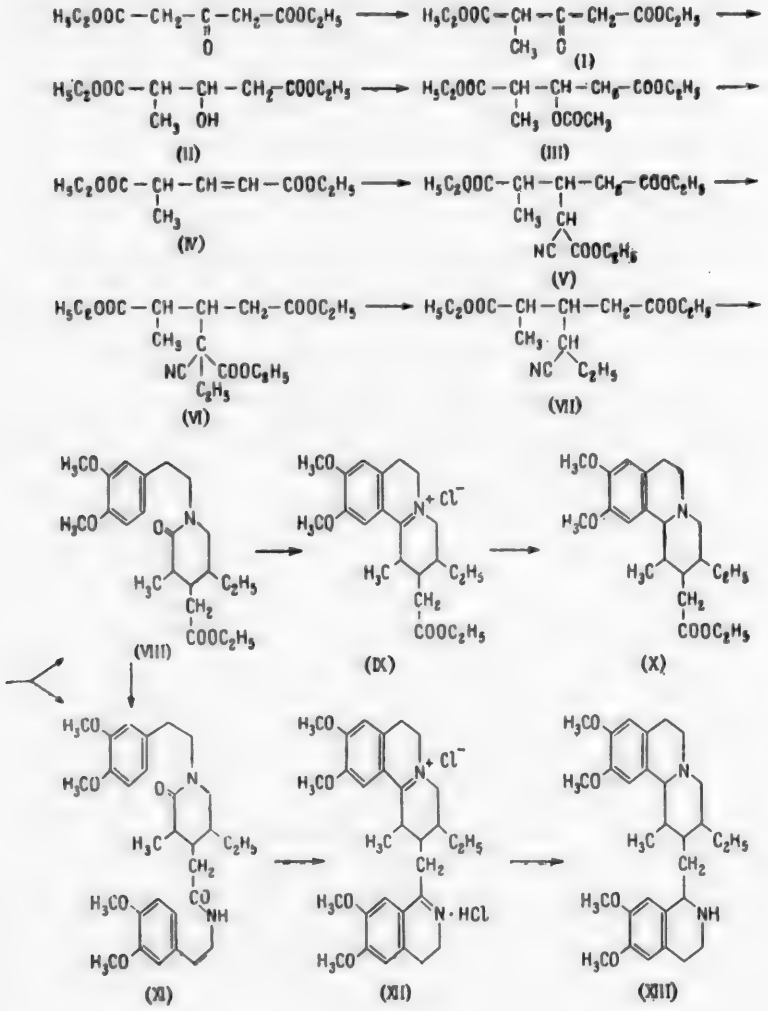
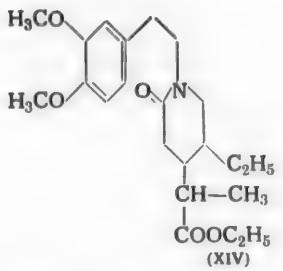
The synthesis of 8-methylemetine was undertaken for the purpose of clarifying the effect of an alkyl substituent on carbon atom C_8 in the emetine molecule on the formation of the rubro-compound. For the preparation of 8-methylemetine a scheme was used that had been developed for emetine [1].



The ethyl ester of acetonedicarboxylic acid was converted by treatment with methyl iodide in the presence of sodium alcoholate to the ethyl ester of α-methylacetonedicarboxylic acid (I). By reduction of the latter in the presence of Raney nickel catalyst the ethyl ester of α-methyl-β-hydroxyglutaric acid (II) was obtained.

The latter upon acetylation with acetic anhydride formed the ethyl ester of α-methyl-β-acetoxyglutaric acid (III). When the acetoxy derivative was heated with potassium acetate the ethyl ester of α-methylglutaric acid (IV) was produced. Further condensation with cyanoacetic ester in the presence of sodium alcoholate led to the ethyl ester of α-methyl-β-(cyano-carboethoxy) methylglutaric acid (V). By treatment with ethyl iodide and sodium alcoholate the latter was converted to the ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy) propylglutaric acid (VI). After selective saponification with the calculated amount of sodium alcoholate and water, the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII) was obtained. Further reductive condensation of this compound with homoveratrylamine led to the piperidone derivative, which might have the structure (VIII) or (XIV).



(XIV)

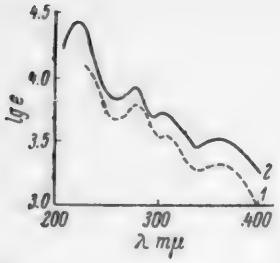
Usually reactions of such a type proceed in the direction of the compounds containing the greatest number of substituents in the ring [2,3], i.e., in the case under consideration we should obtain the piperidone (VIII). Its b. p. 198-199° (0.1 mm) indicated the formation of an individual compound, and not a mixture. The piperidone was converted to the quinolizine derivative (X) by cyclization with phosphorus oxychloride and reduction of the quaternary chloride (IX) obtained in the presence of Raney nickel catalyst. The quinolizine base was isolated as an oil. The anhydrous hydrochloride was an amorphous material; the crystal hydrate was a crystalline substance.

We attempted to demonstrate the position of the methyl group by carrying out an ester condensation of the piperidone (VIII) or the quinolizine derivative (X) with ethyl formate. The reaction did not take place in either case. The negative result could be explained either by the presence of the methyl group not in the ring, but on the side chain, or by steric hindrances occasioned by the presence of a substituent in the ortho position. Ester condensation with the formate also did not occur in the case of the ethyl ester of 4',5'-dimethoxy-6-ethyl-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizyl-7-acetic acid, in which the methyl group is absent. The negative result in this case is dependent, apparently, on steric hindrances. Accordingly, the reaction in the first instance, most probably, also does not occur because of steric hindrances and consequently structure (VIII) should be accepted for the piperidone.

By further condensation of the piperidone (VIII) with homoveratrylamine the diamide (XI) was obtained, which can also be prepared directly by the condensation of the methyl ester of β-(α'-cyano) propylglutaric acid with homoveratrylamine without isolation of the piperidone. The diamide was isolated as a thick yellow oil. By further cyclization with phosphorus oxychloride, the chloride of 4',5'-dimethoxy-6-ethyl-8-methyl-7-(1''-methyl-6'',7''-dimethoxy-3'',4''-dihydroisoquinolyl)-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizine (XII) was obtained, which then was reduced in the presence of Raney nickel catalyst to 8-methylemetine (XIII). The base was isolated as a light yellow oil. By treatment of its ether solution with ether saturated with hydrogen chloride, the hydrochloride was obtained as a colorless, amorphous powder. We did not succeed in isolating the crystalline hydrochloride because of its very great solubility in alcohol.

The rubro-compound was not obtained by oxidation of the base 8-methylemetine (XIII) with bromine and iodine. Oxidation with bromine yielded a slightly yellowish substance, and on oxidation with iodine a yellow amorphous material was obtained. The ultraviolet spectra of these materials(Figure) greatly suggest the spectra of the salts of o-methylpsychotrine which, as is well known, is an intermediate product of the oxidation of emetine to rubroemetine.

Thus the presence of an alkyl substituent on carbon atom C_8 prevents the formation of the rubro-compound. This confirms the participation of carbon atom C_8 in the process of formation of rubroemetine from emetine.



Ultraviolet absorption spectra in alcohol: 1) products of oxidation of 8-methylemetine with iodine, 2) product of oxidation of 8-methylemetine with bromine.

EXPERIMENTAL

Ethyl ester of α-methylacetonedicarboxylic acid (I). To sodium alcoholate prepared from 12.63 g of sodium and 267.5 ml of anhydrous ethyl alcohol were added 105.7 g of the ethyl ester of acetonedicarboxylic acid and 148.2 g of methyl iodide. The mixture was kept gently boiling for 3 hours. After cooling, the alcohol was distilled off in vacuo. To the residue was added 100 ml of water, and the oil that separated was extracted with benzene. The extract was dried with sodium sulfate. The benzene was distilled off and the residue was distilled. Yield 99.6 g (89%). The ethyl ester of α-methylacetonedicarboxylic acid was a colorless liquid, soluble in alcohol, ether, benzene, and chloroform, insoluble in water.

B. p. 118-119° (2 mm), d^{20}_4 1.0914, $n^{20}D$ 1.4390, MR_D 52.08; calculated 51.69 (for keto form), 52.74 (for enol form).

Found %: C 55.58, 55.40; H 7.67, 7.36. $C_{10}H_{16}O_5$. Calculated %: C 55.5; H 7.40.

Ethyl ester of α-methyl-β-hydroxyglutaric acid (II). 50 g of the ethyl ester of α-methylacetonedicarboxylic acid was hydrogenated in the presence of 3 g of Raney nickel catalyst at 140-150° and 100 atm for 4 hours. After the usual treatment the ethyl ester of α-methyl-β-hydroxyglutaric acid was isolated as a colorless liquid, readily soluble in organic solvents, insoluble in water. Yield 45.2 g (90.5%).

B. p. 115-116° (1.5 mm), d^{20}_4 1.0778, $n^{20}D$ 1.4379, MR_D 53.13; calculated 53.21.

Found %: C 55.71, 55.34; H 8.32, 8.19. $C_{10}H_{18}O_5$. Calculated %: C 55.45; H 8.25.

Ethyl ester of α-methyl-β-acetoxyglutaric acid (III). 36.5 g of the ethyl ester of α-methyl-β-hydroxyglutaric acid and 56 g of freshly distilled acetic anhydride were heated to gentle boiling for 1 hour. The excess acetic anhydride and acetic acid was distilled off in vacuo and the residue was distilled. The ethyl ester of α-methyl-β-acetoxyglutaric acid was a colorless liquid, soluble in alcohol, ether, benzene, and chloroform, insoluble in water. Yield 39.55 g (90.7%).

B. p. 124-125° (2 mm), d^{20}_4 1.0772, $n^{20}D$ 1.4340, MR_D 62.92; calculated 62.57.

Found %: C 55.58, 55.55; H 7.72, 7.58. $C_{12}H_{20}O_6$. Calculated %: C 55.53; H 7.74.

Ethyl ester of α-methylglutaric acid (IV). 32.53 g of the ethyl ester of α-methyl-β-acetoxyglutaric acid and 0.156 g of potassium acetate were heated so that acetic acid was distilled off but the temperature of the vapors did not exceed 140°. At the end of the distillation potassium acetate precipitated. Upon cooling the reaction mass was dissolved in ether and the ethereal solution was washed with water. When the acetic acid distillate was diluted with water, an additional amount of oil separated, which was extracted with ether and after being washed was added to the main extract. After the extract was dried with sodium sulfate, the ether was distilled off and the residue was distilled. Yield 25.5 g (88.4%). The ethyl ester of α-methylglutaric acid was a colorless liquid, soluble in the usual organic solvents, insoluble in water.

B. p. 104-105° (2 mm), d^{20}_4 1.0475, $n^{20}D$ 1.4470; MR_D 51.08; calculated 51.22.

Found %: C 60.25, 60.14; H 8.06, 7.83. $C_{10}H_{16}O_4$. Calculated %: C 60.00; H 8.00.

Ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid (V). A mixture of 25.5 g of the ethyl ester of α-methylglutaric acid, 29.2 g of ethyl cyanoacetate, and 20.4 ml of anhydrous ethyl alcohol was heated to gentle boiling for 12 hours. Every 2 hours 1/6 part of the sodium alcoholate prepared from 2.43 g of sodium and 27 ml of anhydrous ethyl alcohol was added. After the usual isolation process the ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid was obtained as a colorless liquid, soluble in the usual organic solvents, insoluble in water. Yield 21.5 g (58.8%).

B. p. 155-156° (1 mm), d^{20}_4 1.1156, $n^{20}D$ 1.4570, MR_D 76.45; calculated 76.25.

Found %: C 57.21, 57.67; H 7.35, 7.44. $C_{15}H_{23}O_6N$. Calculated %: C 57.5; H 7.35.

Ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid (VI). To a solution of sodium ethylate prepared from 3.11 g of sodium and 55.5 ml of anhydrous ethyl alcohol were added 35.5 g of the ethyl ester of α-methyl-β-(cyano-carboethoxy)methylglutaric acid and 40 g of ethyl iodide. The mixture was heated for 1 hour. The ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid was a colorless liquid, soluble in the usual organic solvents, insoluble in water. Yield 30 g (75.5%).

B. p. 158-159° (1 mm), d^{20}_4 1.0904, $n^{20}D$ 1.4600, MR_D 85.65; calculated 85.48.

Found %: C 59.80, 59.79; H 7.76, 7.74. $C_{17}H_{27}O_6N$. Calculated %: C 59.82; H 7.97.

Ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII). To the sodium alcoholate prepared from 3.76 g of sodium and 105.1 ml of anhydrous ethyl alcohol were added 49.1 g of the ethyl ester of α-methyl-β-(α'-cyano-α'-carboethoxy)propylglutaric acid and 2.67 g of water and the mixture was allowed to stand for 12 hours. Then the reaction mass was heated for 1 hour. The excess alcohol was distilled off in vacuo. To the residue was added 50 ml of water and the solution was shaken several times with ether to remove the unsaponified ester. The water layer was acidified with concentrated hydrochloric acid to an acid reaction to Congo. The oil that separated was extracted with ether. The extract was dried with sodium sulfate. The ether was distilled off and the residue was heated at 180° for 40 minutes. Upon cooling it was dissolved in benzene and washed with an aqueous solution of sodium bicarbonate. After the benzene was distilled off, the residue was distilled. Yield 8.17g(24.4%, taking into account the unsaponified ester in the amount of 6.15 g).

The ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid was a thick, colorless liquid, soluble in the usual organic solvents, insoluble in water.

B. p. 130-132° (1 mm), d^{20}_4 1.0754, $n^{20}D$ 1.4690, MR_D 69.70; calculated 69.97.

Found %: C 62.2, 62.75; H 8.89, 8.79; N 5.44, 5.17. $C_{14}H_{23}O_4N$. Calculated %: C 62.43; H 8.63; N 5.24.

Ethyl ester of N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid (VIII). 2.8 g of the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid (VII) in 10 ml of anhydrous ethyl alcohol and 5 g of homoveratrylamine were hydrogenated in the presence of 3 g of Raney nickel catalyst at 90 atm and 110-115° for 2 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in benzene and washed with 3% hydrochloric acid. The benzene was distilled off and the residue was distilled: 1st fraction b. p. 155-190° (0.15 mm), 0.6 g; 2nd fraction b. p. 203-204° (0.15 mm), 1.3 g (32%). Each fraction was redistilled: 1st fraction – unalkylated piperidone (0.45 g), b. p. 145-150° (0.1 mm); 2nd fraction – alkylated piperidone (0.57 g), b. p. 198-199° (0.1 mm).

Found %: C 67.17, 67.15; H 8.32, 8.49; N 3.91, 3.84. $C_{22}H_{33}O_5N$. Calculated %: C 67.49; H 8.5; N 3.58.

Ethyl ester of 4',5'-dimethoxy-6-ethyl-8-methyl-3,4,5,6,7,8-hexahydrobenzo-(1',2':1,2)-quinolizinyl-7-acetic acid (X). 0.35 g of N-alkylated piperidone, 5 ml of anhydrous toluene, and 4 ml of phosphorus oxychloride were heated for 1 hour to gentle boiling. The toluene and phosphorus oxychloride were distilled off in vacuo. The residue was washed with ether and dissolved in 5 ml of 6% hydrochloric acid. The solution was evaporated in vacuo. The chloride was dissolved in alcohol and treated with alcohol saturated with ammonia until the acid reaction to Congo disappeared. The precipitate of inorganic salts was removed. The filtrate was hydrogenated in the presence of Raney nickel catalyst at 70 atm and 75-80° for 2 hours. The catalyst was filtered off and the alcohol was distilled off in vacuo. The residue was dissolved in 5 ml of water and shaken with ether (twice with 5 ml). Then the aqueous solution was treated with ammonia, the oil that separated was extracted with ether, and the extract was dried with sodium sulfate. After the ether was distilled off, a light yellow oil remained. Yield 0.1 g (29.8%). The hydrochloride was obtained by treating an ethereal solution of the base with ether saturated with hydrogen chloride. It was a colorless, amorphous material, readily soluble in alcohol, acetone, and water, insoluble in ether; very hygroscopic. M. p. 126° (deformed at 65°). The hydrochloride was dissolved in 3% hydrochloric acid and the acid solution was evaporated in vacuo. The residue was dissolved in the minimum amount of alcohol and absolute ether was added until there was a slight turbidity. Upon prolonged standing, a white, crystalline precipitate separated out. Before analysis the material was dried for 1 hour at 1 mm and 110°. M. p. 184-185.5° (deformed at 180.5°).

Found %: C 64.05, 63.81; H 7.96, 8.23; N 3.61, 3.62. $C_{22}H_{34}O_4NCl$. Calculated %: C 64.2; H 8.33; N 3.4.

β''-(3'',4''-Dimethoxyphenyl)ethylamido-N-[β'-(3',4'-dimethoxyphenyl)-ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid (XI). 1.2 g of the ethyl ester of α-methyl-β-(α'-cyano)propylglutaric acid dissolved in 15 ml of anhydrous ethyl alcohol and 4.8 g of β-(3,4-dimethoxyphenyl)ethylamine were heated in an autoclave at a hydrogen pressure of 120 atm and 110-115° for 2 hours in the presence of Raney nickel catalyst. After cooling the catalyst was filtered out. The residue after distillation of the alcohol was heated on an oil bath at 180-190° for 3 hours. The cooled reaction mass was carefully washed with ether. The residue was dried in a vacuum desiccator. Yield 1.48 g (95.5). β''-(3'',4''-Dimethoxyphenyl)ethylamido-N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid was a dark yellow, thick oil, soluble in alcohol and chloroform, insoluble in ether.

Found %: C 68.15, 68.29; H 7.94, 7.84; N 5.13, 5.26. $C_{30}H_{42}O_6N_2$. Calculated %: C 68.5; H 8.03; N 5.32.

8-Methylemetine (XIII). A mixture consisting of 1.48 g of β''-(3,''4''-dimethoxyphenyl)ethylamide of N-[β'-(3',4'-dimethoxyphenyl)ethyl]-β-methyl-δ-ethyl-α-piperidone-γ-acetic acid, 25 ml of toluene, and 12.84 ml of freshly distilled phosphorus oxychloride was heated to gentle boiling of the reaction mass for 1 hour. The excess phosphorus oxychloride and toluene was distilled off in vacuo. The residue was washed with absolute ether and dissolved in 10 ml of 6% hydrochloric acid. The solution was evaporated in vacuo to dryness. The residue was dissolved in alcohol and treated with alcohol saturated with ammonia until there was a slight alkaline reaction (to litmus). The precipitate of inorganic salts was removed. The filtrate was hydrogenated in the presence of Raney nickel catalyst at 125 atm and 75-80° for 2 hours. Upon cooling the catalyst was filtered out, the alcohol was distilled off in vacuo, and the residue was dissolved in 10 ml of water, shaken with ether several times, and then neutralized with ammonia. The oil that separated was extracted with ether. The extract was dried with potassium carbonate. After the solvent was distilled off, the base was isolated as a light yellow oil. Yield 0.4 g (28.9%). The hydrochloride was obtained by treating the ether solution of the base with ether saturated with dry hydrogen chloride. It was a colorless, amorphous material, readily soluble in alcohol, acetone, chloroform, and water, insoluble in ether. M. p. 121-122° (deforms at 73°).

Found %: N 4.76, 4.78. $C_{30}H_{42}O_4N_2 \cdot 2HCl$. Calculated %: N 4.93.

Oxidation of 8-methylemetine with bromine. To a solution of 0.18 g of the base 8-methylemetine in 0.36 ml of chloroform were gradually added 0.06 ml of bromine in 1.8 ml of chloroform. The reaction mass was kept at room temperature for 10 minutes, then treated with ammonia solution. After being dried the chloroform was distilled off, the residue was treated with water, the aqueous solution was evaporated in vacuo, and the residue was dissolved in alcohol. When absolute ether was added to the alcohol solution, a slightly yellow precipitate separated out, which was repeatedly washed and dried in a vacuum desiccator. M. p. 195-198° (deformed at 140°).

Found %: N 4.79, 4.96. $C_{30}H_{41}N_2Br$. Calculated %: N 4.85.

Oxidation of 8-methylemetine with iodine. A mixture consisting of 0.2 g of the base 8-methylemetine, 8 ml of anhydrous ethyl alcohol, and 0.4 g of iodine was heated to gentle boiling of the reaction mass for 3.5 hours. Upon cooling the alcohol solution was poured into a solution of sodium bicarbonate. The oily precipitate that formed was washed with sodium hydrosulfite and dissolved in acetone. After the acetone was evaporated in vacuo, the residue was dissolved in alcohol and reprecipitated with ether. M. p. 135-140° (deformed at 119°).

Found %: N 4.48, 4.70. $C_{30}H_{41}N_2I$. Calculated %: N 4.52.

λ_{max} 225 mμ, lgε 4.41; λ 280 mμ, lgε 3.91; λ 310 mμ, lgε 3.71; λ 360 mμ, lgε 3.51; λ_{min} 260 mμ, lgε 3.82; λ 295 mμ, lgε 3.69; λ 340 mμ, lg ε 3.44.

SUMMARY

1. The synthesis of 8-methylemetine has been carried out.

2. It has been shown that the presence of a substituent on the carbon atom C_8 prevents the formation of a rubro-compound.

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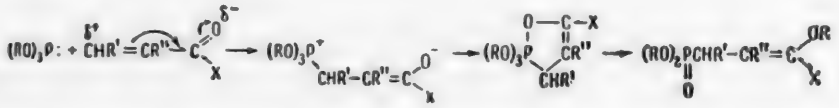
ADDITION OF FULL ESTERS OF PHOSPHOROUS AND PHOSPHINOUS ACIDS TO CONJUGATED SYSTEMS

V. THE PROBLEM OF THE MECHANISM OF THE REACTION OF TRIALKYL PHOSPHITES WITH CONJUGATED SYSTEMS

V. A. Kukhtin and Gil'm Kamai

In previous communications [1,2] we have described a new kind of Arbuzov rearrangement – the reaction of C=C–C=O conjugated systems on esters of phosphorous and phosphinous acids. These reactions proceed according to the general scheme



The reaction mechanism proposed by us assumes preliminary partial ionization of the reacting molecules of the conjugated compound. In this connection it might be supposed that solvents promoting ionization would speed up the addition of phosphites to conjugated systems.

Experiments carried out by us to investigate the intensity of the addition reaction of tributyl phosphite to methacrylic acid in various solvents confirmed this assumption. We investigated the reaction of the above-mentioned reagents, taken in amounts of 0.1 g-mole in different solvents. 33.6 g of solvent was used, i.e., an amount equal to the sum of the starting reagents. All experiments were carried out at 50°. The course of the reaction was checked by the change in refractive index. The end of the reaction was determined by a constant refractive index and the absence of evolution of heat by a sample with Cu_2Cl_2. The completeness of the reaction was determined by distilling off the unreacted methacrylic acid. The data obtained are given in Table 1.

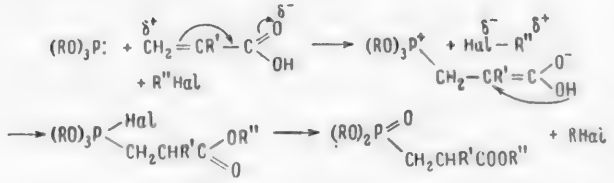
TABLE 1

Solvent	Dielectric constant	Reaction time (in hours)	Percent conversion
Nitrobenzene	36.4	6.5	88
Acetone	21.5	8.5	89.2
Pyridine	12.5	16.5	80
Ether	4.34	18	69
Without solvent	–	10.5	88.5

The experimental data show that the more polar the solvent, the more intensely the reaction proceeds; while solvents having a large dielectric constant speeded up the reaction, weakly polar solvents slowed it down in comparison to the case where the reaction was carried out without a solvent. The results obtained by us may serve to confirm the previously proposed reaction mechanism.

It also appeared to us very interesting to study the combined reaction of alkyl halides and unsaturated acids

with trialkyl phosphites. Alkyl halides, as a rule, are less active in the Arbuzov rearrangement than α,β-unsaturated acids, which react with phosphites even at room temperature and in some cases with considerable evolution of heat. Therefore it might be assumed that in the first stage the phosphite would react predominantly with the α,β-unsaturated acid, and in the second stage, if the mechanism proposed by us corresponds to the actual course of the reaction, the alkyl halide would react actively with the bipolar ion formed or with the intermediate product and the reaction would go according to the scheme



The experiments carried out by us fully confirmed this assumption. Thus, for example, upon reaction of triethyl phosphite with acrylic acid and butyl bromide the butyl ester of β-(diethylphosphono)propionic acid was formed. Similarly, other phosphites, alkyl halides and acids also react in accordance with the above-presented scheme. In Table 3 are given the results of the experiments carried out by us. It is interesting to note that when ethyl bromide and methacrylic acid reacted with tributyl phosphite, in addition to the corresponding ester of β-phosphonoisobutyric acid there also were produced small amounts of butyl methacrylate. In other experiments, although we did not succeed in isolating the pure acrylates, their presence in the reaction products could be assumed because of their characteristic odor. The mechanism of their formation has still not been finally clarified by us.

TABLE 2

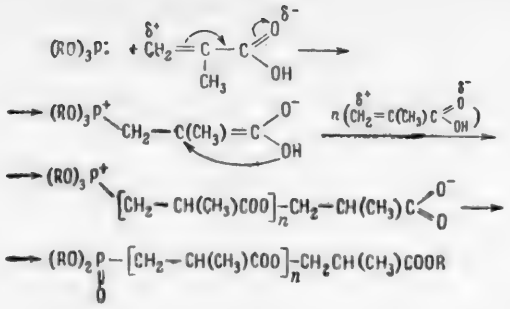
Time (in hours)	$n^{20}D$	Increase in temperature with Cu_2Cl_2	Time (in hours)	$n^{20}D$	Increase in temperature with Cu_2Cl_2
0	1.3938	11°	4.5	1.3919	3.5°
0.5	1.3938	11	5	1.3918	3.5
1	1.3935	10	5.5	1.3920	3
1.5	1.3938	11	6	1.3916	2.5
2	1.3934	8	6.5	1.3916	2.5
2.5	1.3931	7	7	1.3915	2
3	1.3928	6	7.5	1.3912	1
3.5	1.3923	5	8	1.3910	1
4	1.3921	4	8.5	1.3910	1

The results obtained by us confirm the correctness of the previously proposed mechanism for the reaction of trialkyl phosphites with C=C-C=O conjugated systems. The combined reaction of alkyl halides and α,β-unsaturated acids with phosphites also confirms the common reaction mechanism of the above-mentioned reagents with phosphites.

It also is interesting to note that when a reaction was carried out between triethyl phosphite, butyl iodide, and methacrylic acid at room temperature, we were not able to isolate the ester of phosphonoisobutyric acid. At the same time, in the course of the reaction a solid precipitate separated out, which after separation, careful washing, and drying formed a white, powdery, polymeric product at first taken by us to be a polymethacrylate. However, analysis showed that it contained 2.7% phosphorus, from which it was impossible to free it by purification. The formation of such a phosphorus-containing polymer, it seemed to us, might occur by telomerization of triethyl phosphite with methacrylic acid according to the scheme

TABLE 3

Expt. no.	Starting reagents	Products isolated	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	% P found	% P calculated	Yield (in %)
1	1) $CH_2=CHC(=O)OH$	$(C_2H_5O)_2PCH_2CH_2COOC_4H_9$-n	143—146° (8)	1.4330	1.0549	11.66	11.65	17
	2) n-C_4H_9Br	—						
	3) $(C_2H_5O)_3P$	C_2H_5Br	38—40	1.4295	—	—	—	25.6
2	1) $CH_2=C(CH_3)C(=O)OH$	$(n\text{-}C_4H_9O)_2PCH_2CHCOOC_2H_5$ (O, CH_3)	144—146 (3)	1.4344	1.0418	10.2	10.05	21.3
	2) C_2H_5Br	—						
	3) (n-$C_4H_9O)_3P$	$CH_3=C(CH_3)COOC_4H_9$-n	68—70 (21)	1.4280	—	—	—	10.4
3	1) $CH_2=C(CH_3)C(=O)OH$	—						
	2) C_2H_5Cl	$(C_2H_5O)_2PCH_2CHCOOC_2H_5$ (O, CH_3)	146—148 (8)	1.4314	1.0491	11.69	11.71	25.8
	3) $(C_2H_5O)_3P$	—						



With a phosphorus content of 2.7% the polymer obtained should have a molecular weight of approximately 1150. The possibility of telomerization of trialkyl phosphites with methacrylic acid certainly is of great interest and needs further, more detailed investigation.

EXPERIMENTAL

Reaction of tributyl phosphite with methacrylic acid in acetone medium. 25 g of phosphite, 8.5 g of methacrylic acid, and 33.6 g of acetone were heated in a small flask with a reflux condenser and a stirrer at 50°. Every 30 minutes the solution was quickly cooled to 20°, the refractive index was determined, and a test was made for the presence of phosphite with cuprous chloride (0.1 g of Cu_2Cl_2 per 0.2 g of reaction mixture). The results are given in Table 2.

In 8 hrs 30 min the reaction was considered practically completed, and after removal of the solvent the unreacted methacrylic acid was distilled off in vacuo. As a result of the distillation, 0.93 g of acid was isolated (10.8% of the initial amount).

The reaction was carried out in a similar manner in the other experiments. When pyridine was used as the solvent, tests were not made with Cu_2Cl_2, since pyridine reacts with cuprous halide. The yield of the butyl ester of β-phosphonoisobutyric acid was in all cases 40-50%.

Reaction of triethyl phosphite with acrylic acid and butyl bromide. To 20 g of triethyl phosphite and 16.6 g of butyl bromide was added dropwise 8.7 g of acrylic acid. Some time after the beginning of the addition the temperature of the reaction mass started to rise and gradually reached 65-70°. After the evolution of heat ended, the reaction mass was heated on a water

bath for 2 hours. As a result of repeated fractionation 5.4 g of the butyl ester of β-(diethylphosphono)propionic acid was isolated.

B. p. 143-146° (8 mm), $n^{20}D$ 1.4330, d^{20}_0 1.0549, MR_D 62.16; calculated 65.51.

Found %: P 11.69. $C_{11}H_{23}O_5P$. Calculated %: P 11.71.

The remaining experiments were carried out in a similar manner (Table 3).

Reaction of triethyl phosphite with methacrylic acid and butyl iodide. 16.6 g of triethyl phosphite, 8.6 g of methacrylic acid, and 18.3 g of butyl iodide were mixed and left at room temperature. In several hours a flocculent precipitate appeared in the flask. After a day the precipitate was separated, carefully washed with ether, and dried. The weight of the precipitate was 0.78 g. Separation of precipitate continued on the second and third day. In all 2.1 g of precipitate was formed, which after drying and washing was a white powder that did not melt, but gradually turned brown at 200-210°. It was difficultly soluble in acetone, but dissolved readily in alkalized water. In three days the separation of precipitate ceased and the refractive index of the reaction mixture did not change further. It was not possible to isolate individual compounds by fractional distillation of the liquid portion of the reaction products.

Found %: P 2.71; C 53.9; H 7.49. M(Rast method) 1190.
$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}[CH_2CH(CH_3)COO]_{11}CH_2CH(CH_3)COOC_2H_5$. Calculated %: P 2.59; C 54.1; H 7.31. M 1198.

SUMMARY

1. The effect of solvents on the reaction of tributyl phosphite with methacrylic acid has been investigated. It has been established that polar solvents accelerate this reaction.

2. Combined reactions of trialkyl phosphites with α, β-unsaturated acids and alkyl halides have been investigated. The products of their joint reaction have been isolated and a reaction mechanism has been proposed.

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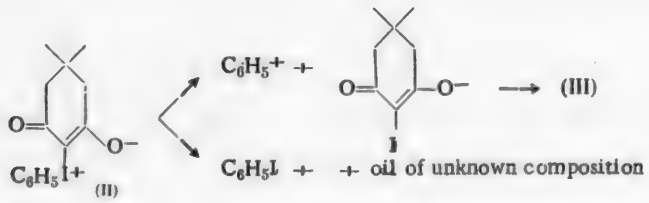
IODONIUM DERIVATIVES OF β-DIKETONES

II. THERMAL DECOMPOSITION OF PHENYLDIMEDONYLIODONE

O. Ia. Neiland, G. Ia. Vanag and E. Iu. Gudrinietse

We have shown [1] that dimedon (5,5-dimethylcyclohexanedione-1,3) (I) reacts very readily with iodosobenzene, forming an iodonium derivative of the enol-betaine type – phenyldimedonyliodone (II). The product after recrystallization and drying in vacuo was completely stable at ordinary temperature, but unpurified phenyldimedonyliodone gradually decomposed in storage. Pure phenyldimedonyliodone decomposes upon prolonged boiling of its aqueous solutions and also when it is boiled in toluene or heated without a solvent above the melting point (139°). It was possible to isolate from the decomposition products iodobenzene and the phenyl ether of iododimedon (III), the composition of which was demonstrated by splitting it with acids to the phenol and converting to the phenyl ether of dimedon (IV). The latter was smoothly split by acids to phenol and dimedon.

The decomposition of phenyldimedonyliodone can be represented by the following diagram.



Depending on the place of rupture of the C–I bond, either the phenyl ether of iododimedon or iodobenzene is obtained.

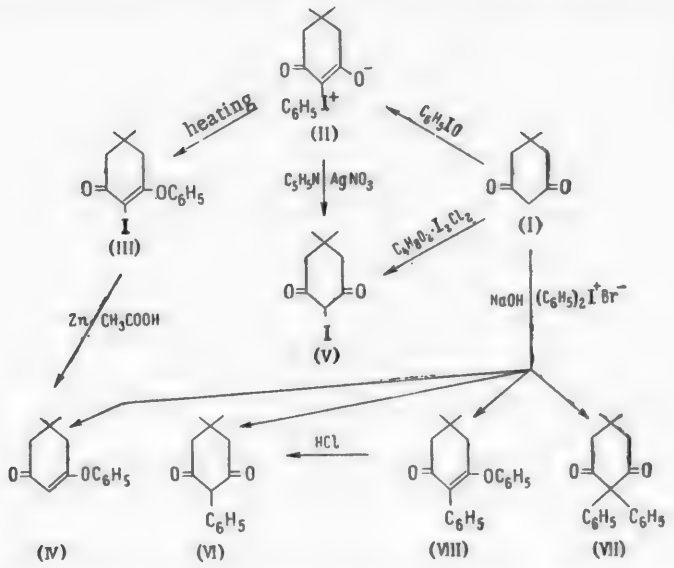
The proposed mechanism for the decomposition of phenyldimedonyliodone is in complete agreement with the already known mechanisms for the decomposition of iodonium salts [2-4].

$$[Ar—I—Ar]^+ + X^- \rightarrow ArI + ArX$$

The decomposition of phenyldimedonyliodone in the presence of pyridine and silver nitrate yielded the silver salt of iododimedon (V), which confirms the suggested scheme for the decomposition with initial formation of an iododimedon anion and a phenyl cation. The formation of N-phenylpyridinium could be demonstrated but considerable amounts of phenol were found. Investigation of the decomposition of phenyldimedonyliodone clearly showed that this compound has an iodonium salt structure.

Phenyl ethers of dimedon have not been described in the literature up to the present time. We attempted to prepare the phenyl ether of dimedon (IV) in another way also – by direct phenylation of dimedon with diphenyliodonium bromide. Although similar reactions are described in the literature [5], they have not been used for the phenylation of β-diketones. We succeeded in isolating all four theoretically possible products – the phenyl ether of dimedon (IV), phenyldimedon (VI), diphenyldimedon (VII), and the phenyl ether of phenyldimedon (VIII), but in small yields (8-18%). The phenyl ether of dimedon (IV) was isolated in insignificant amounts, because it was difficult to purify; however, no depression was observed in a mixed melting point test with previously prepared

material, which permits considering them identical. The structure of diphenyldimedon (VII) was demonstrated by sodium hydroxide fusion. Diphenylmethane and β,β-dimethylglutaric acid were produced. The phenyl ether of phenyldimedon (VIII) was split by the action of acid to phenol and phenyldimedon (VI) (see diagram).



The phenylation reaction of dimedon that was investigated proceeded rapidly and could be used for the preparation of difficultly available phenyl derivatives of dimedon.

EXPERIMENTAL

Phenyl ether of iododimedon (III). 34.2 g of phenyldimedonyliodone (II) was boiled for 1 hour with 300 ml of toluene. The reaction mixture was distilled in vacuo and an iodobenzene fraction was collected with b. p. 63-64° (8 mm), 8.2 g (40%). The residue was washed with 2N potassium hydroxide solution and dried at 100°. Yield 16 g (47%). M. p. 158-162°. The phenyl ether of iododimedon crystallized from glacial acetic acid as yellowish prisms. M. p. 165-166°.

Found %: I 36.98, 37.33. $C_{14}H_{15}O_2I$. Calculated %: I 37.13.

Oxime of the phenyl ether of iododimedon. 0.1 g of the phenyl ether of iododimedon was boiled with 0.4 g of hydroxylamine hydrochloride in 3 ml of pyridine for 2 hours. After dilution with water 0.12 g of precipitate was obtained. It was crystallized from 5 ml of alcohol. Colorless, small needles. M. p. 210° (decomp.).

Found %: N 3.71. $C_{14}H_{16}O_2NI$. Calculated %: N 3.92.

Splitting of the phenyl ether of iododimedon with sulfuric acid. 0.684 g of the phenyl ether of iododimedon was boiled with 10 ml of 50% alcohol and 3 drops of concentrated sulfuric acid for 2 hours. The mixture was diluted with 10 ml of water, filtered off from the tarry materials, and precipitated with bromine water. Yield 0.6 g (91%). The tribromophenol obtained was crystallized from aqueous alcohol. A mixed sample with pure tribromophenol gave no depression in melting point.

Phenyl ether of dimedon (IV). 3.42 g of the phenyl ether of iododimedon (III) was boiled for 2 hours with 35 ml of glacial acetic acid while 15 g of zinc dust was gradually added. The mixture was filtered and diluted with 5 times its amount of water. An emulsion was obtained that slowly started to crystallize. Yield 1.4 g (65%). M. p. 78-80°, b. p. 154-156° (7 mm). After distillation the m. p. was 80-82°. The phenyl ether of dimedon was a white crystalline material, readily soluble in all organic solvents.

Found %: C 77.57; H 7.60. $C_{14}H_{16}O_2$. Calculated %: C 77.78; H 7.41.

Splitting of the phenyl ether of dimedon with hydrochloric acid. 0.108 g of the phenyl ether of dimedon

was boiled with 1 ml of alcohol, 2 ml of water, and 0.3 ml of concentrated hydrochloric acid for 45 minutes. The mixture was diluted with water and several drops of formalin added and it was heated to boiling. Upon cooling, formaldodimedon (methylenebisdimedon) separated. Yield 0.04 g (60%). After crystallization from alcohol the m. p. was 188°. A mixed sample with a pure preparation gave no depression in melting point. According to data in [6] m. p. 189°. By precipitation of the filtrate with bromine water 0.15 g of tribromophenol (90%) was obtained. M. p. 80-83°. The recrystallized product, mixed with pure tribromophenol, gave no melting point depression.

Splitting of phenyldimedonyliodone in the presence of pyridine and silver nitrate. 0.9 g of phenyldimedonyliodone hydrate was dissolved in 10 ml of boiling water, and 1.7 g of silver nitrate and 1 ml of pyridine were added. The mixture was boiled for 15 minutes. After cooling, the precipitate was filtered off and treated with alkali. After removal of the silver oxide and acidification, iododimedon separated out. Yield 0.5 g (75%). M. p. 165° (decomp.). A mixed sample with iododimedon prepared by iodination of dimedon by a complex of iodine chloride with dioxan gave no melting point depression. Tribromophenol was precipitated from the filtrate with bromine water.

Phenylation of dimedon with diphenyliodonium bromide. 7 g of dimedon was dissolved in a mixture of 30 ml of water and 30 ml of dioxan, containing 2 g of sodium hydroxide. To the boiling mixture was gradually added 18 g of diphenyliodonium bromide and all was boiled for 2 hours. At the end of the reaction a layer of yellow oil formed. The mixture was steam distilled to remove the iodobenzene. The residue was treated first with 70 ml, and then with 30 ml of ether. The combined ether extracts were washed twice with 20 ml of 10% potassium carbonate solution and then with 10 ml of water. The ether layer was dried with anhydrous calcium chloride, the ether was distilled off, and the residue was distilled in vacuo and fractions collected with b. p. 150-160° (7 mm) and 160-210° (7 mm).

a) The alkali layer obtained was neutralized with dilute hydrochloric acid and the precipitate was washed with 30 ml of ether and crystallized from 10 ml of alcohol and 20 ml of water. Phenyldimedon (VI) crystallized as lustrous leaflets. Yield 0.92 g (8.5%). M. p. 192-193°.

Found %: C 77.21; H 7.39. $C_{14}H_{16}O_2$. Calculated %: C 77.78; H 7.41.

b) The fraction with b. p. 150-160° (7 mm) was a colorless oil that slowly crystallized. The crystals that formed were pressed out on filter paper, ground to a powder, and dried in vacuo. They were recrystallized from dilute acetic acid. The phenyl ether of dimedon (IV) obtained crystallized as flat prisms. Insignificant yield. M. p. 70-75°. A mixture with the phenyl ether of dimedon prepared from phenyldimedonyliodone melted at 70-78°.

c) The fraction with b. p. 160-210° (7 mm) was a yellow, viscous oil, which was treated with 6 ml of alcohol. The insoluble residue was filtered and washed with alcohol. Yield of diphenyldimedon (VII) 0.6 g (8.2%). M. p. 175-176°. From alcohol – white, flat needles.

Found %: C 81.87; H 6.94. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.85.

d) The alcohol solution (see b) obtained was evaporated. Crystals slowly separated out from the yellow mass and solidified in a week. Yield 1.3 g (17.8%). M. p. 50-60°. The mass was dissolved in glacial acetic acid and precipitated with water. The semicrystalline paste was pressed out on filter paper and recrystallized repeatedly from dilute acetic acid. The phenyl ether of phenyldimedon (VIII) that was obtained formed small prisms. M. p. 85-87°.

Found %: C 81.66; H 7.21. $C_{20}H_{20}O_2$. Calculated %: C 82.19; H 6.85.

2-Nitro-2-phenyldimedon. To a suspension of phenyldimedon (VI) in ether was added several drops of fuming nitric acid until solution was complete. The ethereal solution was washed with water and evaporated. The nitrophenyldimedon crystallized from alcohol as leaflets. M. p. 163-164° (decomp.).

Found %: N 5.56. $C_{14}H_{15}O_4N$. Calculated %: N 5.36.

2-Iodo-2-phenyldimedon. 0.11 g of phenyldimedon (VI) and 0.2 g of a complex of iodine chloride and dioxan were dissolved in 2 ml of glacial acetic acid. Upon dilution of the solution with water 0.14 g (40%) of iodo-phenyldimedon precipitated. M. p. 85-87°. The compound crystallized from alcohol as yellow, flat

needles. M. p. 89-91°.

Found % I 37.45. $C_{14}H_{15}O_2I$. Calculated % I 37.13.

Splitting of diphenyldimedon (VII). A small amount of diphenyldimedon was fused with sodium hydroxide. An oil separated with an odor of mandarin peel – diphenylmethane, which was extracted with carbon tetrachloride and oxidized with chromyl chloride to benzophenone [7]. The semicarbazone melted at 163-164°. A mixed sample with pure benzophenone semicarbazone [8] gave no melting point depression. The alkaline mass was neutralized with hydrochloric acid, evaporated to dryness, and extracted with hot benzene. Upon cooling, β,β-dimethylglutaric acid crystallized with m. p. 100-102°. A mixed sample with pure β,β-dimethylglutaric acid gave no melting point depression.

Splitting of the phenyl ether of phenyldimedon (VIII). An alcohol solution of compound (VIII) was boiled with several drops of hydrochloric acid for 2 hours. When diluted with water, phenyldimedon (VI) separated out as lustrous leaflets. M. p. 188-190°. The recrystallized product mixed with pure phenyldimedon gave no melting point depression. From the filtrate tribromophenol was precipitated with bromine water. M. p. 85-88°. A mixed sample with pure tribromophenol gave no melting point depression.

SUMMARY

1. Upon thermal decomposition of phenyldimedonyliodone a new compound was formed – the phenyl ether of iododimedon; besides this, iodobenzene and an oily material of unknown composition are obtained.

2. The products of the thermal decomposition of phenyldimedonyliodone confirmed its iodonium structure.

3. By reduction of the phenyl ether of iododimedon a new product was obtained – the phenyl ether of dimedon.

4. By direct phenylation of dimedon with diphenyliodonium bromide new products were obtained – the phenyl ether of dimedon, phenyldimedon, diphenyldimedon, and the phenyl ether of phenyldimedon.

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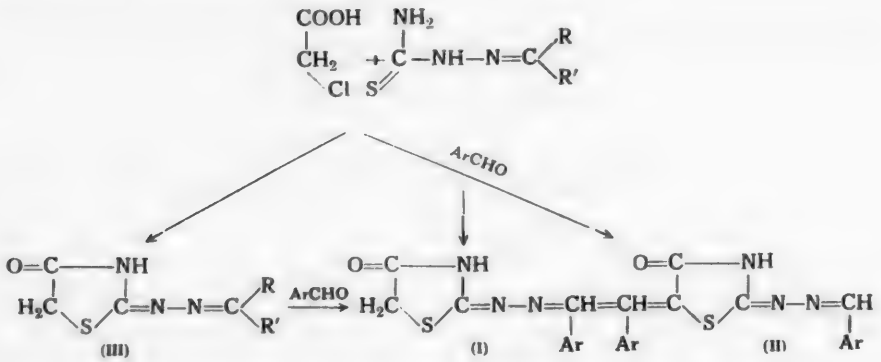
SYNTHESIS OF THIAZOLIDONE DERIVATIVES HAVING BIOLOGICAL INTEREST

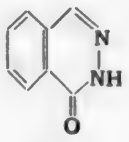
VIII. REPLACEMENT OF SOME RADICALS OF OXO-COMPOUNDS BY OTHERS IN THE MOLECULES OF DERIVATIVES OF THIAZOLIDINEDIONE-2,4-HYDRAZONE-2

N. M. Turkevich and E. V. Vladzimirskaia

In previous communications [1-3] we described for the first time the synthesis of 5-arylidene monoderivatives and 5-arylidene bisderivatives of thiazolidinedione-2,4-arylidenehydrazones-2. In that work we made attempts to prepare analogous derivatives of thiazolidinedione-2,4-alkylidenehydrazones-2, which led to the establishment of new rules for the synthesis of thiazolidine derivatives. It appeared that when the thiosemicarbazones of oxo-compounds of the aliphatic and hydroaromatic series are heated with monochloroacetic acid in the presence of aromatic aldehydes, the expected 5-arylidene derivatives are not formed, but the substitution of the oxo-compounds mentioned by arylidene groups ensues (see diagram). As a result, various 2''-arylidene derivatives of thiazolidinedione-2,4-hydrazone-2 (I) were obtained, which are presented by us in Table 1. As concerns the thiosemicarbazones of the oxo-compounds of the aromatic series, we observed the replacement of some of the arylidene groups by others only in the case of heating of a mixture of the thiosemicarbazone of p-isopropylbenzaldehyde with monochloroacetic acid and p-nitrobenzaldehyde, whereupon thiazolidinedione-2,4-p-nitrobenzylidenehydrazone-2 was obtained (see Table 1).



When the thiosemicarbazones of butyraldehyde and of acetone were introduced into the condensation reaction with monochloroacetic acid in the presence of benzaldehyde, we observed the formation of the 5,2''-dibenzylidene derivative (II, Ar=C_6H_5). The identical compound was synthesized by us [3] by the condensation of thiosemicarbazide with monochloroacetic acid in the presence of an excess of benzaldehyde.



(IV)

TABLE 1

Expt. no.	Thiosemicarbazone	Aromatic aldehyde	Condensation product	Melting point	Yield (in %)	Analysis for N (in %)	
						found	calc.
1	Glucose	Benzaldehyde	(I), Ar=C_6H_5	257—258°	55	19.54	19.17
2	Menthone	Benzaldehyde	(I), Ar=C_6H_5	259	87.5	19.19	19.17
3	Cyclohexanone	Benzaldehyde	(I), Ar=C_6H_5	252	76	18.78	19.17
4	Glucose	Anisaldehyde	(I), Ar=p-$CH_3OC_6H_4$	254—255	64.5	16.90	16.86
5	Glucose	Salicylaldehyde	(I), Ar=o-HOC_6H_4	>300	89.5	17.88	17.86
6	Menthone	Salicylaldehyde	(I), Ar=o-HOC_6H_4	>300	95	17.82	17.86
7	Chloral	Salicylaldehyde	(I), Ar=o-HOC_6H_4	>300	70.5	18.01	17.86
8	Glucose	m-Nitrobenzaldehyde	(I), Ar=m-$O_2NC_6H_4$	270	72	21.05	21.20
9	Chloral	m-Nitrobenzaldehyde	(I), Ar=m-$O_2NC_6H_4$	272	69	21.15	21.20
10	Glucose	o-Chlorobenzaldehyde	(I), Ar=o ClC_6H_4	255	88.5	16.58	16.56
11	Menthone	o-Chlorobenzaldehyde	(I), Ar=o-ClC_6H_4	255	95	16.60	16.56
12	Cuminal	p-Nitrobenzaldehyde	(I), Ar=p-$O_2NC_6H_4$	270	98	21.26	21.20
13	Butyraldehyde	Benzaldehyde	(II), Ar=C_6H_5	283	47	13.72	13.60
14	Acetone	Benzaldehyde	(II), Ar=C_6H_5	283	40	13.90	13.60
15	Acetone	Aldehydophthalic acid	(IV)	185	82	19.32	19.17

The condensation of the thiosemicarbazone of acetone with monochloroacetic acid in the presence of aldehydophthalic acid led to the formation of phthalazone (IV) which gave no depression with a preparation obtained by the method of Gabriel et al.[4].

Replacement of some groups of oxo-compounds by others was observed by us not only upon condensation of monochloroacetic acid with thiosemicarbazones in the presence of aromatic aldehydes, but also upon reaction of aromatic aldehydes with prepared aliphatic and hydroaromatic derivatives of thiazolidinedione-2,4-hydrazone-2 (III), which were synthesized by us by the method of Chabrier et al [5] (see diagram). The results of the pertinent studies are presented in Table 2.

For the identification of the condensation products obtained we synthesized various thiazolidinedione-2,4-arylidenehydrazones-2 [5]. Of these, the 2''-o-chlorobenzylidene- and 2''-m-nitrobenzylidene derivatives have not been described in the literature up to the present time. In all cases a mixed melting point test of the same condensation products prepared by the various methods did not give any depression. Because of the fact that the reaction products with salicylaldehyde (see Table 1 and 2) melt above 300°, their identification was carried out by means of the ultraviolet absorption spectra. The results of the investigations showed that the preparations referred to were identical with respect to absorption maxima and intensities with thiazolidinedione-2,4-salicylidenehydrazone-2 prepared by the method of Chabrier et al.(after 3 recrystallizations from glacial acetic acid the preparation did not melt, as Chabrier indicates, at 255°, but its melting point was above 300° [3]).

EXPERIMENTAL

Equimolecular amounts (12.5 millimoles) of thiosemicarbazone, aromatic aldehyde, and monochloroacetic acid were refluxed in 50-80 ml of glacial acetic acid for 1-2 hours. After the reaction mixture was diluted with a saturated solution of CH_3COONa, the condensation product was filtered off and recrystallized from acetic acid, with the exception of phthalazone, which was recrystallized from water. In the case of the use of the thiosemicarbazones of glucose and chloral for the condensation, the reaction was carried out for 6 hours in alcohol.

We obtained the hydrate of the thiosemicarbazone of chloral first in 77.5% yield by mixing a hot solution of 0.1 g of thiosemicarbazide in 25 ml of water with a cold solution of 16.6 g of chloral hydrate in 20 ml of

TABLE 2

Experiment No.	Substituent in position 2'' of init. prod. (III)	Aromatic aldehyde	Condensation product	Melting point	Yield (in %)	Analysis for N (in %)	
						Found	Calculated
1	Isopropylidene	Benzaldehyde	(I), Ar=C_6H_5	257°	62	19.12	19.17
2	Cyclohexylidene	p-Anisaldehyde	(I), Ar=p-$CH_3OC_6H_4$	255	66	16.92	16.86
3	n-Butylidene	Salicylaldehyde	(I), Ar=o-HOC_6H_4	>300	66	17.70	17.86

water, with subsequent shaking of the mixture until it cooled. The precipitate was filtered off and recrystallized from water. M. p. 90° (decomp.).

Found % N 17.62, 17.51. $C_3H_6ON_3SCl_3$. Calculated % N 17.62.

The replacement of some of the groups of the oxo-compounds by others from prepared derivatives of thiazolidinedione-2,4-hydrazone-2 was carried out by refluxing 20 millimoles of the starting material (see Table 2), 16 millimoles of the aromatic aldehyde, and 16 ml of glacial acetic acid for 1 hour. From the solution formed at first the reaction product separated out after some time as a precipitate which was filtered off, washed with water, and recrystallized from acetic acid.

SUMMARY

1. By the condensation of thiosemicarbazones of the aliphatic or hydroaromatic series with monochloroacetic acid in the presence of aromatic aldehydes, 2''-monoarylidene- or 2'',5-diarylidene derivatives of thiazolidinedione-2,4-hydrazone-2 are produced.

2. Upon the reaction of derivatives of thiazolidinedione-2,4-hydrazone-2 of the aliphatic or hydroaromatic series with aromatic aldehydes, the replacement of some groups of the oxo-compounds by others is observed.

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A NEW METHOD OF SYNTHESIZING ESTERS OF PHOSPHINIC AND THIOPHOSPHINIC ACIDS

XXIX. THE ADDITION OF DIALKYL PHOSPHOROUS ACIDS TO ESTERS OF VINYLACRYLIC AND SORBIC ACIDS AND 3,5 HEPTADIENE-2-ONE

A. N. Pudovik and I. V. Konovalova

As we previously showed, the addition of dialkyl phosphorous acids to esters of α,β-unsaturated carboxylic acids and α,β-unsaturated ketones leads to the formation of esters of phosphone carboxylic acids and phosphone ketones [1]. The reactions with dialkyl thiophosphorous acids and acid esters of alkyl and aryl phosphinic acids [2] proceed in a similar manner. The present paper describes the results of an investigation of the addition reactions between dimethyl phosphorous and diethyl phosphorous acids and the ethyl esters of β-vinylacrylic and sorbic acids, 3,5-heptadiene-2-one and the diethyl ester of butadiene phosphinic acid. Alcoholates of the alkali metals were used as catalysts in these reactions. All the reactions take place very vigorously and are accompanied by a considerable thermal effect. As a result of the addition of diethyl phosphorous acid (in excess) to the ethyl ester of β-vinylacrylic acid addition products of one and two acid molecules were obtained, i.e., the ethyl esters of 4-(diethylphosphone)butene-2-carboxylic acid (I) and 2,4-di-(diethylphosphone) butane carboxylic acid (II).

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}-CH_2-CH=CH-CH_2COOC_2H_5$$
(I)

$$(C_2H_5O)_2\overset{\overset{O}{\|}}{P}-CH_2-CH_2-\underset{\underset{O=P(OC_2H_5)_2}{|}}{CH}-CH_2-COOC_2H_5$$
(II)

The structure of (I) was proven by ozonization. Acetaldehyde was identified in the form of the condensation product with dimedone. Formaldehyde was not found. Acetaldehyde can obviously be formed only from the ester of formylacetic acid as a result of its saponification and decarboxylation, which take place under the conditions of decomposition of ozonides (heating with water).

The addition of diethyl phosphorous acid to the ethyl ester of sorbic acid also leads to the formation of two products (III) and (IV).

$$CH_3-\underset{\underset{O=P(OC_2H_5)_2}{|}}{CH}-CH_2-CH=CH-COOC_2H_5$$
(III)

$$CH_3-\underset{\underset{O=P(OC_2H_5)_2}{|}}{CH}-CH_2-\underset{\underset{O=P(OC_2H_5)_2}{|}}{CH}-CH_2-COOC_2H_5$$
(IV)

The substance (III) contains only one double bond and is the addition product of one molecule of diethyl phosphorous acid. After its ozonization ethyl glyoxylate and acetaldehyde were identified in the form of condensation products with dimedone. Only a small amount of acetaldehyde was found. Acetaldehyde can evidently be formed directly from the ozonide of the α,β-addition product or from the ester of formylacetic acid, as indicated above, in the case of the presence of the α,δ-addition product. The conclusion may, therefore, be drawn from the results obtained that (III) is mainly a γ,δ-addition product containing α,β- or α,δ-forms or both together. The presence of the ester of formylacetic acid in its enol form in the decomposition products of ozonides was qualitatively confirmed by the reaction with ferric chloride.

(IV) does not contain a double bond and is the addition product of two molecules of diethyl phosphorous acid and ethyl sorbate, the ethyl ester of 2,4-di-(diethylphosphone) pentacarboxylic acid.

As a result of the addition of diethyl phosphorous acid and 3,5-heptadiene-2-one an addition product (V), containing one double bond, was obtained.

$$CH_3-\underset{\displaystyle O=P(OC_2H_5)_2}{\underset{|}{CH}}-CH_2-CH=CH-CO-CH_3$$

(V)

After the ozonization of (V) methyl glyoxal was identified in the form of its dimedone derivative; from this the conclusion may be drawn that (V) is 6-(diethylphosphone)-3-heptene-2-one. Similar results were also obtained with dimethyl phosphorous acid. In conclusion, we carried out the addition of diethyl phosphorous acid and the ethyl ester of butadiene phosphinic acid. A 48% yield of the reaction product, di-(diethylphosphone)-butene, was obtained. The position of the double bond in it was not established.

EXPERIMENTAL

The Addition of Dialkyl Phosphorous Acids to Ethyl β-Vinylacrylate

1. The addition of diethyl phosphorous acid. An alcoholic solution of sodium ethylate was added gradually to the reaction mixture consisting of 19 g of diethyl phosphorous acid and 16.2 g of β-vinylacrylic acid (a slight excess of diethyl phosphorous acid was used). The reaction proceeded extremely vigorously and the flask was cooled with water. 10.5 g of the ethyl ester of (diethylphosphone)-butene-2-carboxylic acid (I) and 13.5 g of the ethyl ester of 2,4-di-(diethylphosphone)-butane carboxylic acid (II) were obtained by distillation.

(I) B. p. 167-168° (10 mm), 174-176° (18 mm), $n^{20}D$ 1.4489, d^{20}_4 1.0851, MR_D 65.15; calculated 65.04.

Found %: P 11.91, 11.99. $C_{11}H_{21}O_5P$. Calculated %: P 11.74.

(II) B. p. 235-237° (12 mm), $n^{20}D$ 1.4510, d^{20}_4 1.1262, MR_D 96.16; calculated 96.57.

Found %: P 15.18, 15.13. $C_{18}H_{32}O_8P_2$. Calculated %: P 15.42.

Ozonization. Ozonized oxygen was passed through a solution of 5.5 g of the ethyl ester of 4-(diethylphosphone)-butene-2-carboxylic acid in 22 ml of carbon tetrachloride for 24 hours. After the distillation of the carbon tetrachloride the ozonide was decomposed by heating with water. The volatile decomposition products were trapped in a 50% aqueous-alcoholic solution of dimedone. After recrystallization the white crystalline precipitate had an m. p. of 142°. A mixed melt of this substance and the condensation product of acetaldehyde and dimedone showed no depression of the melting point.

2. The addition of dimethyl phosphorous acid. The reaction was carried out with 4.4 g of dimethyl phosphorous acid and 5 g of ester in the presence of sodium methylate. 3.5 g of the ethyl ester of 4-(dimethylphosphone)-butene-2-carboxylic acid was obtained.

B. p. 172-173° (11 mm), $n^{20}D$ 1.4552, d^{20}_4 1.1528, MR_D 55.58; calculated 55.81.

Found %: P 12.70, 13.22. 87% double bond. $C_9H_{17}O_5P$. Calculated %: P 13.13.

The Addition of Dialkyl Phosphorous Acids to Ethyl Sorbate

1. The addition of diethylphosphorous acid. The reaction was carried out with 19 g of diethyl phosphorous

acid and 19 g of ethyl sorbate in the presence of sodium ethylate and was accompanied by a considerable liberation of heat. As a result of distillation 16.5 g of the ethyl ester of (diethylphosphone)-pentene carboxylic acid (III) and 11 g of the ethyl ester of 2,4-di-(diethylphosphone)-pentene carboxylic acid (IV) were obtained.

(III) B. p. 165-166° (10 mm), $n^{20}D$ 1.4500, d^{20}_4 1.0638, MR_D 70.25; calculated 69.67.

Found %: P 10.37, 11.03. 83% double bond. $C_{12}H_{23}O_5P$. Calculated %: P 11.15.

(IV) B. p. 222-224° (10 mm), $n^{20}D$ 1.4551, d^{20}_4 1.1240, MR_D 100.2; calculated 99.47.

Found %: P 14.69. $C_{16}H_{34}O_8P_2$. Calculated %: P 14.90.

The saponification of (III) and (IV) was carried out in dilute hydrochloric acid in sealed tubes at 130°. In both instances the acids obtained were thick, viscous, straw-colored liquids which did not crystallize on long standing.

Ozonization. Ozonized oxygen was passed for 40 hours through a solution of 5 g of (III) in 20 ml of carbon tetrachloride, the mixture being cooled with snow. The carbon tetrachloride was drawn off under vacuum and water was added to the residue which was then heated gently on a water bath. The volatile decomposition products were gradually transferred to an aqueous-alcoholic solution of dimedone. A small amount of the dimedone derivative of acetaldehyde with an m. p. of 141° (mixed melt 141°) was obtained; the main product was the dimedone derivative of ethyl glyoxylate with an m. p. of 124°.

2. The addition of dimethyl phosphorous acid. 6 g of acid and 8.5 g of ethyl sorbate were used for the reaction. In the presence of sodium methylate the reaction took place with intense liberation of heat from the reaction mixture. A large amount of tar was formed. As a result of two distillations 3.5 g of the ethyl ester of dimethylphosphone pentene carboxylic acid was obtained.

B. p. 170-171° (20 mm), $n^{20}D$ 1.4585, d^{20}_4 1.1311, MR_D 60.33; calculated 60.42.

Found %: P 12.70, 12.35. 85% double bond. $C_{10}H_{19}O_5P$. Calculated %: P 12.40.

The Addition of Dialkyl Phosphorous Acids to 3,5-Heptadiene-2-One

1. The addition of diethyl phosphorous acid. The reaction was carried out with 9 g of ketone and 11.5 g of diethyl phosphorous acid in the presence of sodium ethylate. The temperature of the reaction mixture rose to 92°. The alcoholate was added for as long as its addition resulted in the liberation of heat from the reaction mixture. As a result of two distillations 10 g of 6-(diethylphosphone)-3-heptene-2-one (V) was obtained.

B. p. 163-164° (14 mm), $n^{20}D$ 1.4549, d^{20}_4 1.0542, MR_D 63.72; calculated 63.40.

Found %: P 12.72, 12.90. 84% double bond. $C_{11}H_{21}O_4P$. Calculated %: P 12.50.

Ozonization. 5 g of the product was ozonized in 20 ml of carbon tetrachloride for 50 hours. The ozonide was decomposed by heating with water. Methyl glyoxal was found in the decomposition products; the dimedone derivative of this substance has an m. p. of 165°. A mixed melt with the dimedone derivative of methyl glyoxal (obtained by ozonization of mesityl oxide) showed no depression of the melting point.

The addition of dimethyl phosphorous acid. 13.5 g of dimethyl phosphorous acid and 13.5 g of ketone were used for the reaction. 7 g of 6-(dimethylphosphone)-3-heptene-2-one and a considerable amount of tar were obtained.

B. p. 153-155° (11 mm), $n^{20}D$ 1.4635, d^{20}_4 1.1184, MR_D 54.23; calculated 54.17.

Found %: P 13.86, 13.92. 93% double bond. $C_9H_{17}O_4P$. Calculated %: P 14.09.

As a result of the saponification of 6-(dimethylphosphone)-3-heptene-2-one with dilute hydrochloric acid phosphoneheptenone was obtained in the form of a viscous liquid which did not crystallize on standing.

The addition of diethyl phosphorous acid to the diethyl ester of butadiene-1,3-phosphinic acid. The reaction was carried out with 10.5 g of the ester of butadiene-1,3-phosphinic acid and 7.5 g of diethyl phosphorous acid in the presence of sodium ethylate. The reaction proceeded very vigorously. 8.6 g of di-(diethylphosphone)-butene was obtained.

B. p. 215-216° (10 mm), $n^{20}D$ 1.4559, d^{20}_4 1.1280, MR_D 78.91; calculated 78.88.

Found %: P 18.78. 83% double bond. $C_{12}H_{25}O_5P_2$. Calculated %: P 18.90.

SUMMARY

The addition of dimethyl phosphorous and diethyl phosphorous acids to diene systems, activated by an electronegative group, was investigated: these systems were represented by the ethyl esters of β-vinylacrylic, sorbic and butadiene phosphinic acids and 3,5-heptadiene-2-one.

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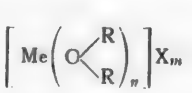
AN INVESTIGATION OF THE THERMAL DECOMPOSITION OF ETHERATES OF MAGNESIUM IODIDE

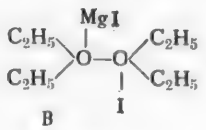
I. ON THE CHEMISM OF OXONIUM COMPOUNDS

V. I. Esafov

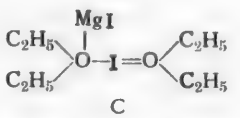
The chemical nature of etherates of metal haloid salts is examined either from the aspect of A. Werner's theory of oxonium salts [1] (formula A), adhered to by B. N. Menshutkin [2] who called these etherates "molecular compounds," or from the aspect of A. Bayer's theory of oxonium compounds. The second of these aspects was supported by N. D. Zelinskii [3] who suggested one of three possible structures (B-D) for the dietherate of magnesium iodide which he obtained, giving preference to formula (D).



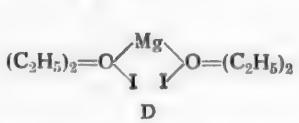
A



B



C



D

Later, N. S. Tsonev [4], who prepared various dietherates of $SnCl_4$, subjected several of these to thermal decomposition assuming that this would provide knowledge of their chemical structure; the investigation was, however, not completed. The method of the thermal decomposition of etherates of the haloid salts of different metals was subsequently used by many chemists [5], principally for carrying out syntheses.

The present investigation was undertaken with the object of determining the strength of the bonds of the ether molecules in the indicated compounds; the thermal decomposition method which must be given preference over other purely chemical methods was also used for this investigation.

We established that with magnesium iodide aliphatic and aliphatic aromatic ethers give dietherates (type 1) which decompose on heating to give magnesium iodide and the corresponding ether. In this connection, ethers differ widely from each other even within the limits of a homologous series. Whereas $(C_2H_5)_2O$* gives the same magnesium iodide dietherate irrespective of whether it is obtained from magnesium iodide itself or a mixture of magnesium and iodine, $(C_4H_9)_2O$, iso-$(C_5H_{11})_2O$, and also $C_6H_5OC_2H_5$ give, in addition to dietherates of the 1st type, dietherates of the 2nd type which are obtained by the action of ethers on a mixture of magnesium and iodine or by an exchange reaction.

$$2\ ROR + MgI_2 \cdot 2(C_2H_5)_2O \longrightarrow MgI_2 \cdot 2ROR + 2(C_2H_5)_2O$$

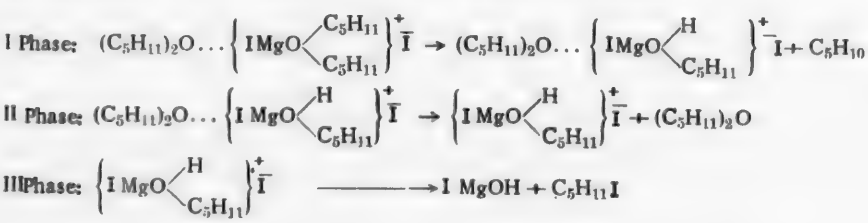
As a result of the thermal decomposition of dietherates of the 2nd type only half the ether is recovered and the other half undergoes fundamental changes. At the same time half the iodine used for the formation of magnesium iodide remains combined with the magnesium. Oxygen compounds of magnesium are found in the

* Evidently $(CH_3)_2O$ and $C_2H_5OCH_3$ also.

dry residues from the decomposition of dietherates of this type; this is proven by the fact that ammonia is liberated when the dry residues are triturated with moist ammonium chloride.* On the basis of experimental data dietherates of the 2nd type must be considered as oxonium salts with structure (I) or (II).

(I) (II)

The problem as to whether they are formed simultaneously in known proportions or whether only one salt, say (II),** is first formed, undergoing rearrangement on heating to salt (I), remains open. When $MgI_2 \cdot 2(C_4H_9)_2O$ decomposes unstable 2,3-diiodobutane is formed; this is best explained on the basis of formula (II). The general course of the decomposition of this dietherate and of $MgI_2 \cdot 2$ iso-$(C_5H_{11})_2O$, in particular, is, however, in closest agreement with the system in which the initial substance is given structure (I).



I Phase: $(C_5H_{11})_2O\ldots \{IMgOR_2\}^+\bar{I} \rightarrow (C_5H_{11})_2O\ldots \{IMgOHR\}^+\bar{I} + C_5H_{10}$

II Phase: $(C_5H_{11})_2O\ldots \{IMgOHR\}^+\bar{I} \rightarrow \{IMgOHR\}^+\bar{I} + (C_5H_{11})_2O$

III Phase: $\{IMgOHR\}^+\bar{I} \longrightarrow IMgOH + C_5H_{11}I$

It is possible that the second molecule of ether which is less firmly combined or becomes so on heating, splits off at the very commencement of decomposition and is retained in the reaction mass, being a substance with a rather high boiling point; the character of the entire system cannot be essentially modified, however, as a result of this. It could be assumed beforehand that when ethers, which give dietherates of the 2nd type with magnesium and iodine, react they do so in the following manner: $ROR + MgI_2 \rightarrow RI + ROMgI$.

In this case the alkyl iodides would be distilled first; they are, however, distilled at the end of the decomposition after the ethers since they have higher boiling points. Finally, as a result of the decomposition of iso-$C_5H_{11}OMgI \cdot 2(C_2H_5)_2O$ (see below) isoamyl iodide is also formed; in consequence, if an ether gave rise to a mixture of alkyl halide with magnesium halide alcoholate the yields of the alkyl halides must, if not exceed then at least approximate 100% on calculating the conversion of one radical of ether to alkyl halide. Facts do not confirm this hypothesis, however. On the basis of all that has been said above we consider that the proposed system of the conversions of dietherates of magnesium iodide of the 2nd type is confirmed by all the experimental data obtained.

EXPERIMENTAL***

The etherates of MgI_2 were prepared in a tubular Würtz flask from 2.4 g of carefully dried magnesium and 25.3 g of sublimed iodine or from 0.1 mole of MgI_2 and absolutely dry ethers in amounts calculated for obtaining $MgI_2 \cdot 2ROR$. The reaction of magnesium with iodine in the presence of ethers proceeds exothermically at first and requires external cooling; toward the end, however, it is necessary to heat the reaction mass to 60-70° in order to completely dissolve the magnesium. The apparatus for the decomposition of the MgI_2 etherates consisted of the above-mentioned flask in the neck of which a dropping funnel, plugged by a calcium chloride tube, was inserted. The tube served for installing the thermometer, the bulb of which was immersed in the reaction mass. The flask was connected to a condenser at the end of which was an adapter with an outlet pipe. A measuring cylinder was connected to the adapter by a cork; this served to collect the liquid products which passed into the cooling mixture of snow and ice during the experiments. 2 U-tubes containing calcium chloride, a Tishchenko bottle, a wash bottle and another Tishchenko bottle were connected to the outlet pipe of the adapter.

* For purposes of brevity this information is not given for the individual experiments in the experimental section.

** In which, in spite of the symmetrical structure, the bonds of the magnesium with the oxygen may not be of equal strength.

*** With the cooperation of the students G. F. Pologov and D. S. Shliapnikov.

The entire system was connected to a gas meter filled with a saturated solution of common salt. The flask was heated on a bath containing Wood's alloy.

I. Experiments on the decomposition of $MgI_2 \cdot 2(C_2H_5)_2O$.* a) To obtain 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ the above-mentioned amounts of magnesium and iodine were used but in order to accelerate the dissolution of the magnesium 50% more than the standard amount of ethyl ether, i.e., 30 ml, was added. After the excess ether had been removed and the mixture cooled the dietherate crystallized immediately. After the dietherate had been carefully dried in a vacuum desiccator the m. p. was 48-50°.

Found %: I 59.09. $MgI_2 \cdot 2(C_2H_5)_2O$. Calculated %: I 59.30.

0.1 mole of the diethylate of magnesium iodide was decomposed. Its complete decomposition took place at 160-165° (temperature of the bath). As a result a total of 19-20 ml of a liquid slightly colored by iodine was obtained and a dry, white residue was left in the flask. To remove the iodine the liquid extract was shaken with mercury after which it distilled completely at 35°. The liquid had d^{20}_4 0.7138 and dissolved in concentrated hydrochloric acid without leaving a residue. The liquid distillate therefore consisted of one ether and, in consequence, the dietherate of magnesium iodide decomposed into its components. The crystalline dietherate with an m. p. of 48-50° was again readily obtained by adding 20 ml of absolute ether to the dry residue in the flask. The dietherate prepared on this occasion from ready-made MgI_2 decomposed at the above-mentioned temperature into magnesium iodide and ether.

b) The decomposition of $MgI_2 \cdot 2(C_2H_5)_2O$, treated with water.** When 3.6 g of water was added carefully to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ heat was evolved, the crystals disappeared and an amorphous mass was formed. The product obtained was heated to 100°, an average of 10 ml of liquid distilling over during this process; 6.5 g of ethyl ether and 2.0 g of a liquid with a b. p. of 55-73° were isolated from this liquid by fractionation. By subsequent heating to 150° a further 9 g of liquid was distilled, from which 1.2 g of ethyl ether and 12 g of a liquid with a b. p. of 55-74° were obtained. Finally, in the third stage of decomposition from 150-220° 5 ml of liquid intensely colored by iodine, was obtained. The dry residue in the flask weighed 10.5 g. The progress of the decomposition of the dietherate of magnesium iodide, treated with water, indicates that the latter first drives out one molecule of ether from it but that the second molecule of ether undergoes chemical conversion. All the liquid products with a b. p. above 55° were combined together, treated with a solution of hyposulfite, water, concentrated hydrochloric acid (to remove ether), a solution of alkali and water and dried with $CaCl_2$. On the average (of three experiments) 16.5 g of a colorless liquid with a b. p. of 71-72°, d^{20}_4 1.9306 was obtained.

Found %: I 80.81. C_2H_5I. Calculated %: I 81.38.

The yield of ethyl iodide was 52.6%, calculated on the assumption of the complete conversion of both ethyl radicals of the ether molecule into ethyl iodide. A weighed sample of the dry residue*** was treated with boiling water and after it had cooled was carefully acidified with dilute HNO_3. The solution was filtered from the carbonaceous residue which was repeatedly washed with water. The filtrate and the wash water were made up to 250 ml; to determine the iodine ion content 10 ml of the solution was, therefore, taken on each occasion. The titration was carried out with a 0.1 N solution of $AgNO_3$ in the presence of eosin. 62.86% I was found.

II. The reaction of dibutyl, diisoamyl and phenylethyl ethers with MgI_2. 0.2 mole of the above-mentioned ethers was added to 0.1 mole of MgI_2 and to complete the reaction heating was carried out for a long period at 120-130° for the first two ethers and at 140-150° in the case of phenetole. The crystalline substances obtained were subjected to decomposition up to a maximum temperature of 265°. The initial ethers were obtained unchanged in the distillates. Consequently, ethers with ready made MgI_2 yield dietherates which decompose into magnesium iodide and ether.

III. The reaction of dibutyl and diisoamyl ethers with $MgI_2 \cdot 2(C_2H_5)_2O$. In each individual experiment 0.1 mole of the ether with the heavier radicals was added to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$ and heating was carried out for 2.5 hours at 130° (bath) for the first and 150° (bath) for the second ether. During this process the

* With the cooperation of I. D. Frolov.
** With the cooperation of P. N. Gorelov.
*** The analyses of the dry residues in the other experiments were carried out in exactly the same manner.

liquid distilled over, 6.5 g being collected on the average. It distilled at 35° and dissolved completely in concentrated hydrochloric acid. A further 0.1 mole of the appropriate ether was then added and heating was continued at the same temperature until the distillation of the liquid had quite finished; an average of 5.6 g of the latter was collected. This was again ethyl ether with a b. p. of 35° which had been driven out of the compound. Ethers with heavier radicals of a primary character therefore displace ethyl ether from $MgI_2 \cdot 2(C_2H_5)_2O$ molecule by molecule. The $MgI_2 \cdot 2(C_4H_9)_2O$ and $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$ obtained by the exchange reaction were then subjected to decomposition. In view of the fact that the decomposition of similar dietherates leads to exactly the same products obtained from dietherates prepared by the action of dibutyl or diosoamyl ethers on a mixture of magnesium and iodine we give data characterizing the process of decomposition of dietherates obtained by the latter method.

IV. Thermal decomposition of $MgI_2 \cdot 2(C_4H_9)_2O$. Dibutyl ether with the following characteristics was used:

B. p. 139.5-139.9° (739 mm), d^{20}_4 0.7705, $n^{20}D$ 1.3991, MR_D 40.86; calculated 40.67.

Complete solution of the magnesium was obtained by reacting 2.4 g of magnesium and 25.3 g of iodine with 26 g of dibutyl ether. The dietherate obtained in the form of a very viscous dark-colored mass was heated. At 102-105° (in the flask) decomposition commenced with evolution of gas, 370 ml of the latter being collected (16°, 739 mm). Decomposition was completed at 270°. 33.5 g of a liquid distillate, intensely colored by iodine, and 18.1 g of dry residue were obtained. In view of the fact that the gas was decolorized by bromine water it (collected from three experiments) was passed through bromine. The crude dibromide was washed with a solution of alkali, then with water and was dried with $CaCl_2$. After it had been filtered the dibromide was distilled; it passed over completely at 158-160°, corresponding to the properties of 2,3-dibromobutane. The butyl radical forming during the course of decomposition was, therefore, stabilized in the form of butene-2. To remove iodine the liquid distillate was washed with a solution of hyposulfite and water and dried with $CaCl_2$. After 2 days, however, the product became dark again as a result of the liberation of iodine. After a second purification the colorless product evolved iodine and gas (which was found to be butene-2) during distillation.

From these data it is evident that the decomposition of the dietherate was accompanied by the formation of 2,3-diiodobutane from the butene-2 and iodine. To remove this diiodobutane the liquid product was heated until the liberation of butene-2 ceased. The liquid product was then shaken with mercury and was finally distilled in a fractionating column. The following main fractions were obtained: 1st, b. p. 129-131°, d^{20}_4 1.6040, 14 g; 2nd, b. p. 139-140°, d^{20}_4 0.8010, 15 g. The yield of butyl iodide was 76% (calculated assuming the conversion of one butyl radical into butyl iodide). The dry residue contained 75.92% (13.7 g) of iodine and 2.16% carbonaceous residue. This proves that of the two atoms of iodine in the magnesium iodide only one took part in the chemical conversions.

V. The thermal decomposition of $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$. Diisoamyl ether with the following characteristics was used:

B. p. 169.5-170.5° (731 mm), d^{20}_4 0.7803, $n^{20}D$ 1.4090, MR_D 50.11; calculated 49.90.

0.1 mole of $MgI_2 \cdot 2iso\text{-}(C_5H_{11})_2O$, prepared from 2.4 g of magnesium 25.3 g of iodine and 31.7 g of diisoamyl ether was subjected to decomposition. At 135° (in the flask) a readily-boiling liquid began to distill over (first phase of decomposition).* In the 173-185° temperature range (second phase of decomposition)* diisoamyl ether distilled over and, finally, in the 185-260° range (third phase of decomposition)* a heavy liquid (isoamyl iodide) distilled. 42.0 g of liquid distillate was obtained and 16.0 g of dry residue was left in the flask. The following fractions were obtained from the liquid product: 1st fraction, b. p. 28-38°, 3.7 g; 2nd fraction, b. p. 146-148°, 17 g; 3rd fraction, b. p. 168-170°, 16.5 g. After it had been distilled over sodium the product with a b. p. of 28-38° had d^{20}_4 of 0.6570 and an iodine number, according to Hanus, of 274.5. The given fraction therefore consisted of about 75% isoamylene. The high boiling point of the fraction indicated the presence in it of trimethylethylene. To investigate this problem Fraebe and Hochsteller's method [6] was tried. A dibromide which was subsequently boiled with water was obtained from 3 g of the substance with a b. p. of 28-38°. Finally, 1.2 g of a product with a b. p. of 90-94° was obtained; the semicarbazone made from this had an m. p. of 112°. The constants of the substance and the semicarbazone correspond to methyl isopropyl ketone. This proves that the fraction with a b. p. of 28-38° contains trimethylethylene, the dibromide of which is converted to methyl isopropyl ketone when boiled with water. In consequence, at the moment of splitting off the isoamyl radical,

* From the data of special experiments in which the liquid products of the individual phases were obtained.

losing an atom of hydrogen, is stabilized mainly in the form of trimethylethylene. The fraction with a b. p. of 146-148° had d^{20}_4 of 1.4275.

Found %: I 64.47. $C_5H_{11}I$. Calculated %: 64.70.

The yield of isamyl iodide was 85.9%. The fraction with a b. p. of 168-170° had d^{20}_4 of 0.7813 and was the initial diisoamyl ether. The amount of recovered ether indicates that of the two molecules of diisoamyl ether included in the dietherate only one took part in chemical conversions. The dry residue was analyzed; it contained 70.67% (10.74 g) of iodine and 5.08% of a carbonaceous residue.

VI. The thermal decomposition of $MgI_2 \cdot 2C_6H_5OC_2H_5$. Phenetole with the following characteristics was used:

B. p. 165° (722mm), d^{20}_4 0.9622, $n^{20}D$ 1.5077, MR_D 37.33; calculated 37.06.

The dietherate obtained by the reaction of 2.4 g of magnesium, 25.3 g of iodine and 24.5 g of phenetole was subjected to decomposition up to a temperature of 260°; 34.3 g of liquid distillate, containing 6.6 g of free iodine. After the treatment of the distillate with a solution of hyposulfite and water, followed by drying with $CaCl_2$, it was fractionated. Finally, 10.9 g of ethyl iodide with a b. p. of 72-73°, d^{20}_4 1.9083 and 10.5 g of phenetole with a b. p. of 164-166° were obtained. 3 g of crystalline phenol with an m. p. of 40° was extracted from the condenser. The residue in the flask was a dark tarry mass weighing 17.5 g. It contained 41.7% iodine. Taking into account the free iodine liberated and the iodine in the dry residue it is evident that in this instance only half the iodine used for the reaction takes part in the conversions. Likewise, out of two ether molecules one is recovered unchanged.

VII. The thermal decomposition of iso-$C_5H_{11}OMgI \cdot 2(C_2H_5)_2O$. The Grignard reagent prepared from 2.4 g of magnesium and 18 g of CH_3I in 40 ml of absolute ether was heated in a bath at 100° to remove excess ether and methyl iodide. After it had cooled, 8.5 g of anhydrous isoamyl alcohol was carefully added. As a result of this operation 2345 ml* of methane (17°, 732 mm) was obtained. The flask with the etherate was then heated up to 235°; 25.5 ml of liquid extract was obtained; the dry residue in the flask weighed 14.4 g and contained 66.85% iodine. $^2/_3$ of the iodine used for the reaction therefore remained chemically combined with the magnesium. To remove the ethyl ether the liquid distillate was treated with concentrated hydrochloric acid, then with a weak solution of alkali and water and dried with $CaCl_2$. After it had been fractionated the following fractions were obtained: 1st fraction, 32-35°, 2.4 g, d^{20}_4 0.6580 (this fraction reacted vigorously with bromine); 2nd, 70-73°, 1.5 g, d^{20}_4 1.8900; 3rd, 73-146°, 3.2 g; 4th, 146-148°, 2.3 g, d^{20}_4 1.4170. During the course of the decomposition of iso-$C_5H_{11}OMgI \cdot (C_2H_5)_2O$ isoamylene, ethyl iodide and isoamyl iodide were, therefore, obtained. In view of the small amount present the nature of the products included in the intermediate fraction with a b. p. of 73-146° was not investigated in greater detail.

SUMMARY

1. It was established that with MgI_2, ethers give dietherates with a weak bond between the magnesium and the oxygen of the ether molecules, as a result of which they are decomposed on heating into MgI_2 and ether.

2. It was shown that ethers differ among themselves with regard to their capacity to form dietherates of MgI_2 with different properties. Some ethers form the same dietherate of MgI_2 irrespective of whether the latter is made from MgI_2 or a mixture of magnesium and iodine. The second group of ethers gives two types of dietherates of MgI_2: the first of these is obtained from MgI_2, the second from a mixture of magnesium and iodine or by driving out ethyl ether from $MgI_2 \cdot 2(C_2H_5)_2O$.

3. It was shown that ethers with heavier primary radicals displace ethers with lighter radicals from $MgI_2 \cdot 2R_2O$.

4. It was shown that the thermal decomposition of dietherates of MgI_2 of the 2nd type with aliphatic ethers is accompanied by the formation of olefins and alkyl iodides, one molecule of ether and one atom of iodine taking part in the chemical conversions. The second atom of iodine remains firmly combined with the magnesium.

5. It was shown that in the thermal decomposition of dietherates of MgI_2 of the 2nd type with aliphatic-aromatic ethers alkyl halides, phenols and a tarry mass are formed. One molecule of the aliphatic-aromatic ether is liberated in the free state.

* As in original – Publisher's note.

6. The presence of a stable chemical bond between the magnesium and the oxygen of one molecule of ether in dietherates of MgI_2 of the 2nd type indicates their oxonium nature.

7. A system for the thermal decomposition of dietherates of the 2nd type was given.

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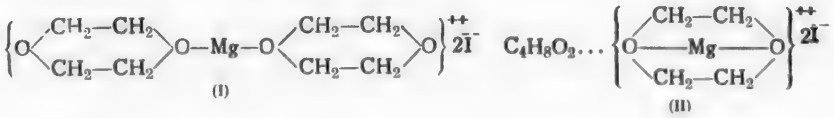
AN INVESTIGATION OF THE THERMAL DECOMPOSITION OF THE REACTION PRODUCTS OF DIOXAN WITH MAGNESIUM IODIDE DIETHERATE, MAGNESIUM IODIDE AND A MIXTURE OF MAGNESIUM AND IODINE

II. ON THE CHEMISM OF OXONIUM COMPOUNDS

V. I. Esafov

The fact having been established that with magnesium iodide, ethers give compounds of the type $MgI_2 \cdot 2ROR$, which decompose on heating into the initial components,* it was worth investigating similar compounds containing dioxan. It was first established that the action of dioxan on $MgI_2 \cdot 2(C_2H_5)_2O$ and $RMgHal \cdot 2(C_2H_5)_2O$ [2] is completely analogous, i.e., the dioxan displaces equimolecular ethyl ether from them. In contrast to ethers the compound which dioxan forms with MgI_2, $MgI_2 \cdot 2C_4H_8O_2$, only liberates half its dioxan on heating and the other half undergoes decomposition. The oxygen atoms of dioxan therefore have a greater capacity for the formation of oxonium salts than the oxygen atoms of ethers and, in consequence, give more stable oxonium compounds. Dioxan gives the most typical oxonium compound when it acts on a mixture of magnesium and iodine. This substance must be considered as a dioxonium salt with a symmetrical (I) or an unsymmetrical (II) structure



(I) (II)

The problem as to whether these salts are formed simultaneously or whether only the (I) salt is initially formed and is then converted to salt (II) on heating remains unsolved. One thing is clear, namely that if salt (I) kept its structure on heating, β,β'-diiododiethyl ether would be found in the decomposition products; this was not found during the experiments. On the contrary, the experimental data are in complete agreement with structure (II). Among the decomposition products of this salt were found dioxan, ethylene, ethylene iodide, ethyl iodide, acetaldehyde, iodine and magnesium oxide. Finally, data on the reaction of dioxan with a mixture of magnesium and iodine prove that like ethers dioxan did not react in this instance according to the system

$$C_4H_8O_2 + MgI_2 \rightarrow C_2H_4I_2 + C_2H_4O_2Mg,$$

because instead of the readily-melting ethylene iodide the infusible dioxonium salt was actually obtained.

EXPERIMENTAL**

1. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$, obtained by the action of dioxan on $MgI_2 \cdot 2(C_2H_5)_2O$. The experiments were carried out in the apparatus described previously [1]. 9 g of absolute dioxan was added with stirring to 0.1 mole of $MgI_2 \cdot 2(C_2H_5)_2O$, heated to 50° and the substance obtained was heated at 115-120°

* See paper I [1].

** With the cooperation of the student V. D. Kharochkin.

until the distillation of the liquid ceased. In this process an average of 9 ml (6.5 g) of liquid distillate was obtained; this distilled almost completely at 35° and dissolved completely in concentrated hydrochloric acid. A further 9 g of dioxan was added to the product, cooled to 50° and the mixture was heated to 125-130° until the distillation of liquid ceased, 10.5 ml (7.8 g) of the latter being obtained on the average; with the exception of a few drops this liquid consisted of ethyl ether. The $MgI_2 \cdot 2C_4H_8O_2$, obtained by driving out ethyl ether, was a white solid product of greatly increased volume which was subjected to decomposition up to a limit of 355°. 1.76 liters of gas (17°, 743 mm), containing 76.3 vol. % ethylene, 12.4 g of a dark-colored liquid distillate, 2.5 g of a crystalline product mixed with iodine and 26.4 g of a dry residue were obtained. The following fractions were obtained from the liquid distillate: 1st, up to 40°, 1.5 g; 2nd, 70-72°, 1.1 g, d^{20}_4 1.8992; 3rd, 99-100°, 7.2 g; the residue was 2.2 g. The 1st fraction gave a positive reaction with fuchsine sulfurous acid, the 2nd fraction consisted of ethyl iodide, the 3rd fraction which did not enter into the reaction with dioxan had a d^{20}_4 of 1.0340. The crystalline substance and the residue from the distillates of the liquid products were treated with a solution of KI until the iodine was completely removed. The solution of iodine in KI obtained required 280.0 ml of a 0.1 N solution of $Na_2S_2O_3$, corresponding to 3.554 g of iodine. After treatment with a solution of KI the crystalline product weighed 0.6 g (see below, Experiment 3). 7.03% carbonaceous residue, 0.72 g of free and 18.76 g of combined iodine were found in the analysis of the dry residue (26.4 g). When the dry residue was triturated with moist ammonium chloride in a mortar ammonia was liberated.

2. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$, obtained by the action of dioxan on MgI_2. 18 g of absolute dioxan was added at 27° to 0.1 mole of MgI_2; the temperature rose by 1°. To complete the reaction the mixture was heated for 6 hours at 80°. Finally, a white solid mass was obtained which was subjected to decomposition up to a limit of 325°. Distillation of the liquid commenced at 94°, the liberation of gas began at 244°. After decomposition 1.2 liters (19°, 743 mm) of gas was obtained; this contained 60.3 vol. % ethylene, 14.8 g of a dark liquid distillate, 1.2 g of a crystalline product (see below, Experiment 3) and 27.0 g of dry residue. As a result of fractionation the following fractions were obtained from the liquid distillate: 1st, up to 40°, 0.3 g, giving a positive reaction with fuchsine sulfurous acid;* 2nd, 70-72°, 0.4 g; 3rd, 99-100°, 10.7 g; 2.1 g of a residue consisting almost entirely of iodine. 5.2% of carbonaceous residue, 2.9 g of free and 20.0 g of combined iodine were found in the dry residue.

3. The thermal decomposition of $MgI_2 \cdot 2C_4H_8O_2$, obtained by the action of dioxan on a mixture of magnesium and iodine. 18 g of absolute dioxan was added in one stage to a mixture of 2.4 g of magnesium and 25.3 g of iodine. The temperature rose by 2.5°. The dioxan was combined with iodine into diiodide, the reaction with magnesium commenced only after the diiodide melted (~85°) and then proceeded with evolution of heat up to 112°. To complete the reaction the reaction mass was then heated for a considerable time at 95-100°. Finally, a spongy, infusible mass was formed from which, as a result of subsequent heating to 200°, an average of 7.5 g of dioxan with a b. p. of 99-100° (737 mm), d^{20}_4 1.0300** was obtained. This fact proves that of the two molecules of dioxan only one is subjected to fundamental chemical conversions. Decomposition was completed at 365°, the temperature being kept within the 355-365° range for 1.5 hours towards the end of the reaction. 1.6 liters of gas (19°, 732 mm), containing 70.2 vol. % ethylene, was obtained. A dibromide was obtained from the gas collected from all the experiments:

B. p. 130-131°, d^{20}_4 2.1757, $n^{20}D$ 1.5315, MR_D 26.51; calculated 26.96.

The liquid distillate contained iodine and a crystalline substance which was filtered through a glass filter. After it had been fractionated the filtrate gave the following fractions: 1st, up to 40°, 0.3 g; 2nd, 70-72°, 1.7 g, d^{20}_4 1.9008; 3rd, 99-100°, 8.4 g, d^{20}_4 1.028, and a residue. The condenser and the adapter of the decomposition apparatus were filled with a crystalline substance mixed with iodine. This mixture, the crystalline substance from the filter and the residue from the fractionations were treated with a solution of KI to remove iodine. The solution obtained contained 9.95 g of free iodine. The crystalline substance was dried in a vacuum desiccator and weighed 8 g. After it had been crystallized from petroleum ether it was obtained in the form of long (>1 cm) colorless needles with an m. p. of 81°; these were analyzed.

Found % I 89.76. $C_2H_4I_2$. Calculated % I 90.05.

The yield of ethylene iodide was 28.3%. The dry residue from the decomposition (14.7 g) contained 6.5 g

* The water in the wash bottles also gave a positive aldehyde reaction.

** Data of a special experiment.

of combined iodine. When it was triturated with moist ammonium chloride ammonia was liberated. The first fractions with a boiling point of up to 40° were mixed with the water from the wash bottles and treated with a solution of $KMnO_4$. The filtrate from the MnO_2 was made alkaline and was evaporated to dryness. The potassium salts were decomposed with dilute sulfuric acid after which the organic acids were steam distilled. The aqueous solution of the latter was saturated with Ag_2CO_3. The solution of the Ag salts was condensed until crystallization commenced. The Ag salt, dried at 85° to constant weight, contained 64.4% Ag. The data obtained prove the presence of acetaldehyde in the water of the wash bottles and the fraction up to 40°.

SUMMARY

1. It was shown that dioxan displaces ethyl ether equimolecularly from $MgI_2 \cdot 2(C_2H_5)_2O$.

2. In contrast to aliphatic and aliphatic-aromatic ethers with MgI_2 dioxan gives an oxonium compound with a more stable bond of the magnesium with the oxygen.

3. It was shown that as a result of the decomposition of $MgI_2 \cdot 2C_4H_8O_2$ half the dioxan is reliberated while the other half forms ethylene, ethylene iodide, ethyl iodide and acetaldehyde.

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THE SYNTHESIS AND INVESTIGATION OF THE CHLORINATION PRODUCTS OF ACETYLENYLDIVINYL (1,3-HEXADIENE-5-INE)

A. N. Akopian, A. M. Saakian and M. G. Avetian

It is known [1] that when vinylacetylene is obtained by the low-temperature polymerization of acetylene a certain amount of divinylacetylene is formed, the actual quantity depending on the conditions of the process. As was shown by A. L. Klebanskii and his co-workers [2], the divinylacetylene obtained contains 15-20% of its isomer, acetylenyldivinyl. The latter was subjected to hydrochlorination [2], hydration [3] and hydrogenation [4]. It was shown that it readily polymerizes and reacts with oxygen twice as rapidly as divinylacetylene, forming explosive peroxides. There are no data in literature on the chlorination of acetylenyldivinyl whereas the chlorination of divinylacetylene has been investigated in detail [5]. It was shown that during the process of the chlorination of divinylacetylene its di-, tetra- and hexachloro derivatives are formed and that the formation of each succeeding compound from the previous one takes place by the addition of chlorine in the 1,4 position, i.e., at the ends of the conjugate enoid compound or diene. It is possible that the cause of this phenomenon is the symmetrical structure of divinylacetylene.

Acetylenyldivinyl is distinguished from divinylacetylene by the unsymmetrical structure of the molecules; it would, therefore, be expected that it would chlorinate in a different manner. In our laboratory it was repeatedly found that divinylacetylene chlorinates far more rapidly than acetylenyldivinyl.

The investigation of the chlorination reaction of acetylenyldivinyl, apart from the preparation and description of the new compounds of this series and the elucidation of the reaction mechanisms, can also be of use if technical divinylacetylene is utilized by means of its chlorination and the subsequent processing of the chloro derivatives.

Depending on the direction of addition of the chlorine, as a result of the chlorination of acetylenyldivinyl the formation of dichloro derivatives with the following structure would be expected:

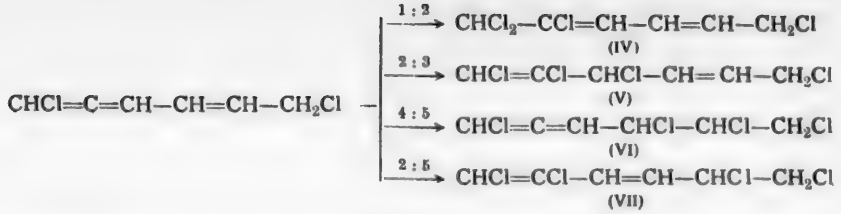
$$HC\equiv C-CH=CH-CH=CH_2 \xrightarrow{1:2} CHCl=CCl-CH=CH-CH=CH_2 \quad (I)$$

$$HC\equiv C-CH=CH-CH=CH_2 \xrightarrow{1:4} CHCl=C=CH-CHCl-CH=CH_2 \quad (II)$$

$$HC\equiv C-CH=CH-CH=CH_2 \xrightarrow{1:6} CHCl=C=CH-CH=CH-CH_2Cl \quad (III)$$

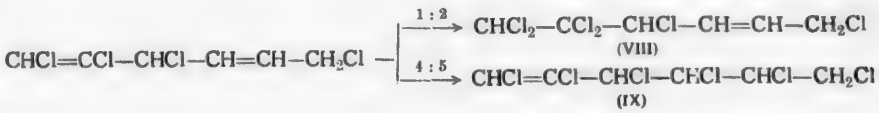
Other possible directions of the reaction, in which the triple bond remains unaffected, do not seem very probable to us. The fact that chloroacetic acid was formed as a result of the oxidation by potassium permanganate of the dichloride obtained from acetylenyldivinyl and that an atom of chlorine was split off by the action of a hot aqueous solution of sodium carbonate on the dichloro derivative indicates that the addition of the first molecule of chlorine to acetylenyldivinyl takes place in the 1,6 position, the result being the formation of 1,6-dichloro-1,2,4-hexatriene (III).

Depending on the direction of addition of the chlorine, the conversion of the dichlorohexatriene formed into the tetrachloride would lead to compounds of the following structure



The formation of chloroacetic acid as the main product in the oxidation by potassium permanganate of the tetrachlorohexadiene formed indicates that the double bond between the 4 and 5 carbon atoms remains unaffected, i.e., substances (VI) and (VII) are out of the question and the decisive factor in the choice between compounds (IV) and (V) is the fact that as a result of the action of a hot aqueous solution of sodium carbonate on the tetrachloride two chlorine atoms are split off; in the conversion of 1,6-dichloro-1,2,4-hexatriene to the tetrachloride the addition of chlorine does not take place at the ends of the conjugate diene but the double bond between the 2 and 3 carbons is saturated, as a result of which 1,2,3,6-tetrachloro-1,4-hexadiene is formed.

The next chlorination product of acetylenyldivinyl is hexachlorohexene which we obtained by the direct chlorination both of acetylenyldivinyl and its tetrachloro derivative. On the basis of the structure of the initial 1,2,3,6-tetrachloro-1,4-hexadiene two hexachlorides (VIII) and (IX) can be expected.



Unfortunately, it is impossible to establish which of these two structures corresponds to the hexachloride obtained because like the hexachloride of divinylacetylene the compound obtained is not oxidized by potassium permanganate, is not acted on by ozone and with continued ozonization splits off hydrogen chloride; this obscures the true picture. The fact that on oxidation with potassium permanganate the dichlorohexatriene and tetrachlorohexadiene preceding the hexachloride form chloroacetic acid while the hexachloride is not oxidized by potassium permanganate and chloroacetic acid is not formed indicates that the double bond between the 4 and 5 carbons has ceased to exist. We assume, therefore, that the structure of the hexachloride corresponds to (IX) and that it is 1,2,3,4,5,6-hexachloro-1-hexene.

In contrast to divinylacetylene which does not undergo complete chlorination even under the influence of sunlight and the final chlorination product of which is 1,2,3,4,5,6-hexachloro-3-hexene, acetylenyldivinyl is completely chlorinated, i.e., it gives octachlorohexane. The preparation of the latter from the hexachloride is carried out in sunlight. From its structure the expected octachloride must be 1,1,2,2,3,4,5,6-octachlorohexane

In consequence, as a result of the chlorination of acetylenyldivinyl the following compounds not described in literature were obtained; 1,6-dichloro-1,2,4-hexatriene, 1,2,3,6-tetrachloro-1,4-hexadiene, 1,2,3,4,5,6-hexachloro-1-hexene and 1,1,2,2,3,4,5,6-octachlorohexane. The di- and tetrachloro derivatives are very unstable liquids with a characteristic unpleasant odor. On keeping, they split off hydrogen chloride and rapidly become turbid and tarry, the first undergoing these changes in the course of several days, the last in a matter of weeks. The hexachloride is a colorless stable oily liquid with a pleasant citrus odor. Octachlorohexane is in the form of lamellar crystals with an odor of camphor.

EXPERIMENTAL

The acetylenyldivinyl was separated from the fraction of divinylacetylene obtained by the low-temperature polymerization of acetylene with Nieuwland's catalyst [1] by a method reported in the work [2]; b. p. 79° (680 mm), d^{20}_4 0.7848, $n^{20}D$ 1.5090.

Formulas of the substances	B. p. or m. p.	d_4^{20}	n_D^{20}	MR_D found	MR_D calculated	Cl content (in %) found	Cl content (in %) calculated
$CHCl{=}C{-}CH{=}CH{-}CH_2Cl$	45—46° (3 mm)	1.1640	1.5309	39.5945	38.241	47.49	47.65
$CHCl{=}CCl{-}CHCl{-}CH{=}CH{-}CH_2Cl$	88—90 (3 mm)	1.4242	1.5572	49.7423	48.442	64.68	64.54
$CHCl{=}CCl{-}CHCl{-}CHCl{-}CH_2Cl$	110—112 (2 mm)	1.5605	1.5491	59.3257	58.643	72.68	73.19
$CHCl_2{-}CCl_2{-}CHCl{-}CHCl{-}CHCl{-}CH_2Cl$	M.p. 124—125°	—	—	—	—	78.1	78.46

The preparation of 1,6-dichloro-1,2,4-hexatriene. Chlorine was passed through a solution of 63 g (0.8 mole) of acetylenyldivinyl in 325 g of CCl_4, cooled externally by ice water, until there was an increase in weight of 60 g (0.84 mole). After the distillation of the solvent the residue was fractionally distilled under vacuum. 1st fraction, b. p. 60-75° (10 mm), 40 g; 2nd fraction, b. p. 75-105° (5 mm), 30 g; 3rd fraction, b. p. 105-130° (5 mm), 20 g; the residue was 25 g of tar.

After repeated distillation the 1st fraction was found to be mainly 1,6-dichloro-1,2,4-hexatriene. The yield was 40%. The 2nd and 3rd fractions consisted mainly of tetra- and hexachlorides, respectively.

The preparation of 1,2,3,6-tetrachloro-1,4-hexadiene. Chlorination was carried out in the manner described above. 40 g of acetylenyldivinyl in 200 g of CCl_4 was used; the chlorine was passed until there was an increase in weight of 62 g. After the solvent had been removed and the 2nd fraction fractionally distilled the latter which had a b. p. of 70-100° (2 mm) (36 g) consisted mainly of tetrachlorohexatriene. The yield was 32%.

The preparation of 1,2,3,4,5,6-hexachloro-1-hexene. a) Chlorine was passed into a solution of 47 g of acetylenyldivinylin 250 g of CCl_4 until there was an increase in weight of 130 g. The following fractions were obtained: 1st fraction, b. p. up to 105° (3 mm), 15 g; 2nd fraction, b. p. 105-120° (3 mm), 76 g; the residue was 75 g of tar. The 2nd fraction consisted mainly of hexachloride. The yield was 45%.

b) A slow current of chlorine was passed through a solution of 14 g (0.063 mole) of 1,2,3,6-tetrachloro-1,4-hexadiene in 70 g of CCl_4 for 20 hours at room temperature. The following were obtained: 1st fraction, b. p. 110-130° (3 mm), 15 g; 2nd fraction, b. p. 130-140° (3 mm), 4 g; the residue was 4 g of tar. Repeated distillation of the 1st fraction gave 11 g (61%) of pure hexachloride.

The preparation of 1,1,2,2,3,4,5,6-octachlorohexane. A solution of 14 g of 1,2,3,4,5,6-hexachloro-1-hexene in 200 g of CCl_4 was saturated, while cooled with ice water, with chlorine (7.5 g) and exposed to sunlight until decolorized. The operation was repeated again with 9.9 g of chlorine. After the solvent had been removed 7 g of crystals with an m. p. of 124-125° (from methanol) was obtained.

The physical properties of the acetylenyldivinylchlorides we obtained and the analytical data are given in Table 1.

The structure of the acetylenyldivinylchlorides was based on the determination of the amounts of saponifiable chlorine atoms in them and by the results of oxidation with potassium permanganate.

a) A mixture of 5 g of dichloride and 7 g of Na_2CO_3 in 100 ml of water was boiled for 9 hours, the mixture being stirred. Analysis of the aqueous layer showed the presence of 0.033 mole of sodium chloride, corresponding to one atom of saponifiable chlorine.

b) 30 g of dichloride in 200 ml of water was reduced at 15° with 202 g of potassium permanganate for 13 hours. After the precipitate of manganese dioxide had been separated and the solution from it acidified 8 g of chloroacetic acid was extracted; after the latter had been recrystallized from petroleum ether the m. p. was 59-60° and it showed no depression of the m. p. in a mixed melt with known chloroacetic acid.

The saponification of tetrachlorohexadiene under the same conditions showed the presence of two atoms of saponifiable chlorine. The oxidation of 30 g of tetrachloride took 120 g of potassium permanganate; 8.3 g of unpurified chloroacetic acid was obtained.

SUMMARY

The chlorination products of acetylenyldivinyl were prepared and investigated. It was shown that chlorination takes place via the formation of 1,6-dichloro-1,2,4-hexatriene, 1,2,3,6-tetrachloro-1,4-hexadiene, 1,2,3,4,5,6-hexachloro-1-hexene and, finally, 1,1,2,2,3,4,5,6-octachlorohexane is obtained.

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THE PREPARATION AND PROPERTIES OF SOME ARYL DERIVATIVES OF THIOXANTHENOL-5-DIOXIDE WITH INDICATOR PROPERTIES

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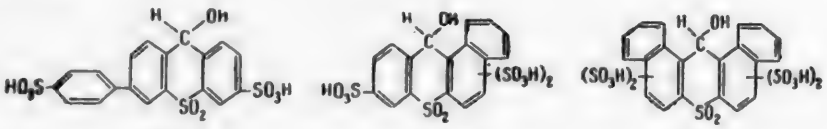
As we have previously communicated [1], under specific conditions derivatives of thioxanthenol-5-dioxide having indicator properties are obtained by the sulfonation of certain aromatic compounds of the type Ar_2CH-R' where R' = H, Alk or Ar. In the development of this work it appeared to us of interest to investigate the influence of various aryl substituents on the color of the compounds obtained during sulfonation and the possibility of using them as indicators in acidimetric determinations. For this purpose we investigated the sulfonation of 4-benzyldiphenyl, α-benzylnaphthalene and α,α'-dinaphthylmethane. The sulfonation was carried out with 25-40% oleum at high temperature. As a result, sulfonic acids having indicator properties similar to those previously described [1], were obtained. In neutral and acid media solutions of these compounds remained colorless, becoming intensely colored on the addition of alkali. The change in the color of these compounds takes place at a pH of 10-11. The color of a particular compound depends on the nature of the substituent; this is evident from the absorption curves in the visible region of alkaline solutions of the above-mentioned compounds (see Fig. 1).*

The compounds obtained were easily oxidized by potassium permanganate and chromic acid, losing their capacity to change color in an alkaline medium. They can be used as indicators for titrations. The absolute error in the titration of various organic acids is on the average ± 0.3%.

On the basis of the properties and the analysis of the compounds obtained their structure can be represented by the formulas (I-III).



(I) (II) (III)

EXPERIMENTAL

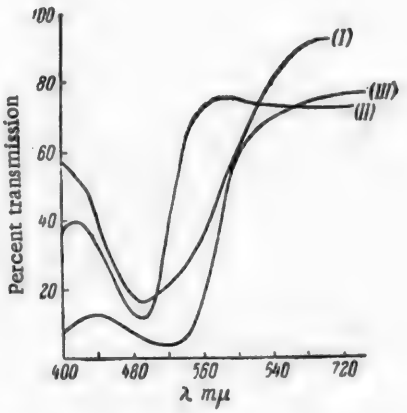
Synthesis of the initial substances. 4-Benzyldiphenyl was synthesized from diphenyl and benzyl chloride in the presence of $ZnCl_2$. For this purpose 250 g of diphenyl 136 g of benzyl chloride and 70 g of $ZnCl_2$ were heated on an oil bath until the liberation of HCl ceased. The product was then extracted with ether and washed with water; after the solvent and the unreacted diphenyl had been distilled under vacuum 90 g of a hydrocarbon with a b. p. of 195-200° (4 mm) and an m. p. of 84-85° (literature data: m. p. 85° [2]) was obtained.

Found %: C 93.30, 93.43; H 6.27, 6.48. $C_{19}H_{16}$. Calculated % C 93.50; H 6.50.

α-Benzylnaphthalene was obtained by a similar method [3]. α,α'-Dinaphthylmethane was synthesized from naphthalene and α,α'-dichlorodimethyl ester in nitrobenzene in the presence of $AlCl_3$, by analogy with a previously described method [4]. For this purpose 170 ml of dry nitrobenzene was introduced into a half-liter, pear-shaped, four-necked flask, equipped with a stirrer, thermometer, reflux condenser and a dropping funnel; 40 g of $AlCl_3$ was then dissolved in the nitrobenzene, cooling being employed. 89 g of pure naphthalene was then added in small portions. A mixture of 20 g of α,α'-dichlorodimethyl ester in 30 ml of nitrobenzene was

* The spectra were determined by A. M. Fisher.

then added dropwise from a dropping funnel over a period of 30 minutes, the mixture being stirred. As a result, the temperature rose from 18 to 37°. The reaction mixture was then heated on a water bath at 45-50° until the liberation of HCl had completely ceased. The contents of the flask were poured into water acidified with HCl, the nitrobenzene layer was washed with alkali and water and the nitrobenzene was steam distilled. The viscous light-yellow mass which remained was recrystallized from alcohol. 80 g (86%) of pure α,α'-dinaphthylmethane with an m. p. of 106-107° was obtained. A mixed melt with the hydrocarbon obtained by means of a Grignard reagent [5] showed no depression of the melting point.



Absorption curves in the visible region of the compounds (I), (II) (Ba salt) and (III) (K salt) in an aqueous solution of NaOH (pH 11.5). (Explanation in the text)

The sulfonation of 4-benzyldiphenyl. 20 g of 4-benzyldiphenyl was treated with 40% oleum, the mixture being stirred until the hydrocarbon layer disappeared. The temperature rose to 180°. The reaction mixture was poured carefully onto ice and neutralized with barium carbonate. The solution was filtered from $BaSO_4$, concentrated, filtered again and the Ba salt (I) precipitated with alcohol; the weight of the precipitate was 42 g (83%). By repeated recrystallization a perfectly pure salt was obtained.

Found %: Ba 22.17, 22.20. $C_{19}H_{12}O_9S_3Ba$. Calculated %: Ba 22.30.

The sulfonation of α-benzylnaphthalene. 25 g of α-benzylnaphthalene (m. p. 53-54°) was treated with 40% oleum until the hydrocarbon layer disappeared, the temperature rising during this process to 165°. The mixture was kept at this temperature for 15 minutes and the cooled sulfonic mass was poured onto ice. After it had been neutralized with $BaCO_3$ and filtered the solution was concentrated under vacuum and the Ba salt (II) was precipitated with alcohol. 62 g of salt was obtained, representing a yield of 70%. The ammonium salt (II) was obtained by precipitating the Ba^{2+} with a saturated solution of $(NH_4)_2SO_4$.

Found %: NH_4 9.20, 9.18. $C_{17}H_{21}O_{12}N_3S_4$. Calculated %: NH_4 9.20.

Found %: Ba 27.52, 27.65. $(C_{17}H_9O_{12}S_4)_2Ba_3$. Calculated %: Ba 27.82.

The sulfonation of α, α'-dinaphthylmethane. 9.77 g of α,α'-dinaphthylmethane (m. p. 108-109°) was treated with 63 g of 25% oleum, the mixture being cooled. It was then heated to 120° and kept at this temperature for 20 minutes. The mass was cooled and poured onto ice. It was neutralized with $BaCO_3$, filtered, concentrated on a water bath and the Ba salt (III) was precipitated with alcohol, the weight obtained being 24 g (71.0%). The ammonium salt was also prepared and analyzed.

Found %: Ba 29.43, 29.12. $C_{21}H_{10}O_{15}S_5Ba_2$. Calculated %: Ba 29.20.

Found %: NH_4 9.55, 9.60. $C_{21}H_{10}O_{15}S_5(NH_4)_4$. Calculated %: NH_4 9.80.

SUMMARY

1. A method was developed for synthesizing sulfonic acids of thioxanthenol-5-dioxide derivatives by the sulfonation of 4-benzyldiphenyl, α-benzylnaphthalene and α,α'-dinaphthylmethane with oleum at high temperature.

2. It was shown that the above-mentioned compounds can be used as indicators for acidimetric determinations.

3. A simple method was developed for synthesizing α,α'-dinaphthylmethane from naphthalene and α,α'-dichlorodimethyl ester in a medium of nitrobenzene in the presence of $AlCl_3$.

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TRIAROXYPHOSPHAZOACYLS

A. V. Kirsanov, G. I. Derkach and R. G. Makitra

Triaroxyphosphazoacyls of the type of $RCON{=}P(OR')_3$ are similar in formula and nature to the readily accessible and fairly well studied triaroxyphosphazo compounds of the type of $RSO_2N{=}P(OR')_3$ [1]. Nevertheless there are also profound differences between them due to the fundamental differences in the chemical characters of the $RCO-$ and RSO_2- residues. The similarity between triaroxyphosphazoacyls and triaroxyphosphazosulfo compounds is manifested in a series of general chemical properties and also in the fact that they can be prepared by similar reaction schemes:

$$RCON{=}PCl_3 + 3NaOR' \rightarrow 3NaCl + RCON{=}P(OR')_3 \quad (I)$$

$$RSO_2N{=}PCl_3 + 3NaOR' \rightarrow 3NaCl + RSO_2N{=}P(OR')_3 \quad (II)$$

Their behavior on heating and hydrolysis reveals the principal fundamental differences in the chemical nature of triaroxyphosphazoacyls (I) and triaroxyphosphazosulfo compounds (II). Depending upon the nature of the radical R, compounds (I) more or less easily split off the corresponding triester of phosphoric acid when heated and gave nitriles (compare [2]) according to the equation

$$RCON{=}P(OR')_3 \rightarrow OP(OR')_3 + RCN \quad (III)$$

Reaction (III) goes quickly at room temperature in presence of hydrogen chloride as catalyst (compare [3]). Compounds (II) are remarkably resistant to heating, and hydrogen chloride has no action on them. No case has hitherto been known of thermal cleavage of compounds (II) by a mechanism similar to the cleavage of (III), although such a cleavage cannot be altogether excluded in principle. This difference is undoubtedly due to nitriles being thermodynamically favored and to compounds of the type of $RSO{\equiv}N$ being thermodynamically unfavored. It may be mentioned, however, that in one case a compound of this type (more correctly its trimer) could be obtained by thermal cleavage of the acid chloride of trichlorophosphazosulfuric acid [4].

Compounds (II) are easily saponified by caustic alkalies with formation of salts of the diesters of the corresponding alkyl- or arylsulfonamidophosphoric acids [5], but they are substantially not hydrolyzed by water in neutral solutions. No difficulties therefore arise in the preparation and isolation of compounds (II). Compounds (I) are hydrolyzed with amazing ease (compare [6]). When a bottle containing crystalline triphenoxyphosphazobenzoyl (IV) is opened, a waxy film quickly forms on the surface of the crystals and the substance absorbs moisture from the air and is quickly transformed into a semiliquid mixture of phenol and the diphenyl ester of benzoylamidophosphoric acid. Liquid triphenoxyphosphazo-p-nitrobenzene (VI) quickly turns cloudy in contact with atmospheric moisture and soon deposits crystals of the corresponding diester. Boiling of all of substances (I) with 96% alcohol substantially hydrolyzes them to the diesters of the acylamidophosphoric acids. The preparation, isolation and purification of triaroxyphosphazoacyls is therefore associated with great experimental difficulties, and arrangements must be made to exclude atmospheric moisture. This marked difference is evidently due to the fact that hydrolysis of triaroxyphosphazoacyls (I) in alkaline solutions involves participation of carbon and oxygen atoms of the carboxyl group, thus increasing the positive charge of the phosphorus atom in accordance with the equation

TABLE 1

Triaroxyphosphazoacyls $ArCON{=}P(OAr')_3$ (I)

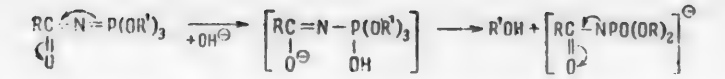
Substance no.	Ar	Ar'	Crystallization medium, form of crystals	Yield (%)	Melting point	Found (%) N	Gross formula	Calculated (%) N
IV	C_6H_5	C_6H_5	Ligroine, stout prisms	80.3	74—76°	3.20	$C_{25}H_{20}O_4NP$	3.26
V	α-$C_{10}H_7$	C_6H_5	Ligroine, prisms	82.0	60—63	2.99	$C_{29}H_{22}O_4NP$	2.91
VI	p-$NO_2C_6H_4$	C_6H_5	Liquid	83.9	—	5.84	$C_{25}H_{19}O_6N_2P$	5.91
VII	3,5-$(NO_2)_2C_6H_3$	C_6H_5	Ligroine, aggregates of prisms	78.5	87—89	8.36	$C_{25}H_{18}O_8N_3P$	8.10
VIII	2-Cl-4-$NO_2C_6H_3$	C_6H_5	Liquid	79.1	—	5.41	$C_{25}H_{18}O_6N_2PCl$	5.52
IX	p-ClC_6H_4	α-$C_{10}H_7$	Benzene + ligroine, prisms	73.4	156—158	2.30	$C_{37}H_{25}O_4NPCl$	2.29
X	3,5-$(NO_2)_2C_6H_3$	p-ClC_6H_4	Benzene, rhombohedra	82.0	150—152	7.01	$C_{25}H_{15}O_8N_3PCl_3$	6.75
XI	p-$NO_2C_6H_4$	o-$NO_2C_6H_4$	Benzene + ligroine, light-yellow needles	79.7	130—133	11.66	$C_{25}H_{16}O_{12}N_5P$	11.49
XII	3,5-$(NO_2)_2C_6H_3$	CH_3	CCl_4 prisms	84.0	68—70	12.81	$C_{10}H_{12}O_8N_3P$	12.61

TABLE 2

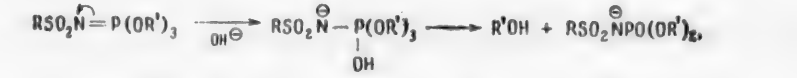
Diesters of Acylamidophosphoric Acids $ArCONHPO(OAr')_2$ (XIII)

Ar	Ar'	Form of crystals	Yield (%)	Melting point	Found		Gross formula	Calculated*
					N (%)	calc.		N (%)
C_6H_5	C_6H_5	Prisms	96.1	147—149°	see [6]	—	—	—
α-$C_{10}H_7$	C_6H_5	Plates	97.0	127—129	3.59	1.00	$C_{23}H_{18}O_4NP$	3.48
p-$NO_2C_6H_4$	C_6H_5	Prisms	97.0	151—152	see [6]	—	—	—
3,5-$(NO_2)_2C_6H_3$	C_6H_5	Prisms	99.0	197—199	9.51	0.97	$C_{19}H_{14}O_8N_3P$	9.50
2-Cl-4-$NO_2C_6H_3$	C_6H_5	Prisms	93.4	107—109	6.50	0.98	$C_{19}H_{14}O_6N_2PCl$	6.48
p-ClC_6H_4	α-$C_{10}H_7$	Prisms	94.9	165—167	3.04	1.00	$C_{27}H_{19}O_4NPCl$	2.88
3,5-$(NO_2)_2C_6H_3$	p-ClC_6H_4	Needles	98.1	216—217	8.42	0.98	$C_{19}H_{12}O_8N_3PCl_2$	8.36
p-$NO_2C_6H_4$	o-$NO_2C_6H_4$	Light-yellow prisms	95.3	178—179	[6]	—	—	—
3,5-$(NO_2)_2C_6H_3$	CH_3	Needles	98.1	189—191	13.40	1.01	$C_9H_{10}O_8N_3P$	13.15

*Equivalent calc.: 1.0.



In the main only the nitrogen and phosphorus atoms participate in the mechanism of hydrolysis of triaroxyphosphazosulfo compounds in alkaline solutions:



for the sulfur and oxygen atoms of the sulfo group cannot appreciably increase the positive charge of the phosphorus atom since the $S^{VI}=N$ bond is extraordinarily unfavored (compounds containing the $S^{VI}=N$ bond are nearly unknown), and therefore conjugation between the $O=S^{VI}$ and N=P bonds is improbable.

Triphenoxyphosphazobenzoyl (IV) and triphenoxyphosphazo-p-nitrobenzoyl (VI) were also synthesized by the action of the corresponding azides on triphenyl phosphite (compare [7]) according to the equation:

$$ArCON_3 + P(OC_6H_5)_3 \rightarrow [ArCON{=}N{-}N{=}P(OC_6H_5)_3] \rightarrow N_2 + ArCON{=}P(OC_6H_5)_3$$

Compounds (IV) and (VI) prepared by this route were found to be identical with the products obtained from trichlorophosphazoacyls and sodium arylates, so that their structure is established. The remaining properties of the triaroxyphosphazoacyls are presented in Table 1 and in the experimental part.

EXPERIMENTAL

All of the operations from start to end of the synthesis of triaroxyphosphazoacyls must be performed as far as possible under conditions excluding reaction with moisture of the air. The nature of the acyl radical in the aromatic ring evidently has little influence on the rate of hydrolysis. The nature of the ester radicals plays a much more important part. Triphenoxyphosphazoacyls (IV-VIII) are especially easily hydrolyzed; compound (X) is hydrolyzed with slightly more difficulty and compound (XI) with appreciably more difficulty; but even (XI) is rapidly transformed into the corresponding diester when kept in 96% alcohol in the air. The exceptional ease of hydrolysis of compounds (I) enabled the diesters of aromatic acylamidophosphoric acids to be prepared from trichlorophosphazoacyls and sodium arylates in good yields without isolation of compounds (I) [6].

Triphenoxyphosphazobenzoyl (IV). To a solution of 0.025 mole of trichlorophosphazobenzoyl in 40 ml of dioxane was added rapidly (with vigorous stirring) a suspension of 0.075 mole of finely pulverized and thoroughly dried sodium phenate in 50 ml of dioxane. A fair amount of heat was liberated and the reaction was completed in 4-5 minutes. The precipitated sodium chloride was removed by centrifuging (in closed vessels) and the dioxane was distilled off in vacuo. The residue was a colorless liquid which crystallized completely at 0° after 2-3 hours. The product (IV) was purified by recrystallization from ligroine.

Compounds (V-VIII) were similarly prepared. Liquid (VI) and (VIII) were purified by reprecipitation from benzene or dioxane solutions by addition of ligroine.

Tri-α-naphthoxyphosphazo-p-chlorobenzoyl (IX). 0.03 g-atom of sodium was added to a solution of 0.03 mole of α-naphthol in 70 ml of ether. After the whole of the sodium had dissolved, a solution of 0.01 mole of trichlorophosphazo-p-chlorobenzoyl in 40 ml of ether was slowly stirred in. The reaction went with evolution of heat. After the whole of the chloride had been added, stirring was continued for another 10-15 minutes. The mixture was then heated to the boil and the sodium chloride filtered off. On cooling, the solution deposited (IX) as fine prisms. Part of the (IX) remained in the precipitated sodium chloride and could be extracted by boiling with ether.

Tri-p-chlorotriphenoxyphosphazo-3,5-dinitrobenzoyl (X). To a mixture of 30 ml of ether, 20 ml of benzene and 0.045 mole of sodium p-chlorophenate was gradually added a solution of 0.015 mole of trichlorophosphazo-3,5-dinitrobenzoyl in 40 ml of benzene with continuous stirring. The reaction went with fairly considerable

release of heat, and the reaction mixture immediately turned brown, but the color disappeared at the end of the reaction (10-15 minutes). The mixture was gently heated, the sodium chloride was separated by centrifuging, and the solvent was distilled off in vacuo. The residue was an oil that crystallized at once. Part of (X) remained in the sodium chloride precipitate from which it could be extracted with boiling ether.

Tri-o-nitrotriphenoxy-p-nitrobenzoyl (XI). A mixture of 0.02 mole of trichlorophosphazo-p-nitrobenzoyl, 0.062 mole of pulverized sodium o-nitrophenate and 50 ml of benzene was refluxed for 1 hour, the sodium chloride and excess of sodium nitrophenate were suction-filtered, and the benzene was distilled off in vacuo. The residue was crystalline (XI).

Trimethoxyphosphazo-3,5-dinitrobenzoyl (XII). A solution of 0.06 mole of sodium methoxide in 40 ml of methanol was cooled to 0°, and a solution of 0.02 mole of trichlorophosphazo-3,5-dinitrobenzoyl in 50 ml of benzene was added with vigorous stirring at such a rate that the temperature of the mixture was maintained at 0 to +5°. The reaction mixture was then heated to the boil, the sodium chloride was separated by centrifuging and the solvent was distilled off in vacuo. 1 to 2 ml of ligroine was added to the liquid residue. After 2-3 hours' standing at 0°, compound (XII) crystallized completely.

All of compounds (I) are readily soluble in dioxane, poorly soluble in cold ligroine and very much more soluble at the boil. Compounds (IX) and (XI) are sparingly soluble in cold ether; all the others are easily soluble. The majority of compounds (I) crystallize nicely from ligroine or from a mixture of benzene and ligroine; (XII) crystallizes from CCl_4.

Cleavage of triaroxyphosphazoacyls according to equation (III) easily takes place on heating or at room temperature in presence of hydrogen chloride. 0.05 mole of (IV) was placed in a small Claisen flask, and dry hydrogen chloride was charged in. After 24 hours the crystalline (IV) had completely liquefied. The benzonitrile was distilled off in a vacuum of about 1 mm (26-37°) and redistilled without vacuum in a small column; b. p. 188.5-189.5°; yield 86%. It was identified by its melting point, specific gravity and refractive index. The residue after the first distillation of benzonitrile was recrystallized from alcohol to give triphenyl phosphate (yield 82%) with m. p. 49-50°; it was identified in a mixed melting test.

0.05 mole of (IV) was distilled in vacuo and the following fractions were collected: 74-90° (13 mm, benzonitrile); 90-240° (intermediate, 2.5 g); 240-244° (10 mm, triphenyl phosphate). Redistillation of the first fraction gave 89.5% of pure benzonitrile (b. p. 188.5-189.5°); redistillation of the last fraction gave 68.5% of pure triphenyl phosphate (m. p. 49-50°). All of the other compounds (I) were cleaved in similar fashion.

Hydrolysis of triaroxyphosphazoacyls to diesters of acylamidophosphoric acids (XIII). Hydrolysis was effected by mixing compounds (I) with water or by exposing to the air in a thin layer. (XIII) was most conveniently prepared by boiling compounds (I) with an aqueous alcoholic solution of sodium hydroxide or with 96% alcohol. Table 2 contains the yields of (XIII) obtained by boiling (I) (0.01 mole) with 50 ml of 96% alcohol for 1 hour. Compounds (XIII) were purified by recrystallization from aqueous alcohol.

The newly prepared compounds (XIII), like those previously synthesized [6], are acidic crystalline substances that titrate with phenolphthalein like monobasic acids. They are very sparingly soluble in hot water (the dimethyl ester is very much more soluble) and ether, easily soluble in benzene, acetone, dioxane; they can be recrystallized from alcohol.

Reaction of benzoyl azide with triphenyl phosphite. A mixture of 0.01 mole of benzoyl azide, 0.01 mole of triphenyl phosphite and 15 ml of ether was refluxed for 2 hours; the ether was driven off on a water bath. A thermometer was inserted in the residual liquid which was slowly heated. Nitrogen started to come off at 80°; a violent reaction commenced at 110°, and then the external heating was stopped. Due to the heat of reaction the temperature of the liquid rose to 160°. After the liquid had cooled, 10 ml of ligroine and a seed crystal of (IV) were added. Crystals quickly deposited and were suction-filtered and washed with ligroine. The triphenoxyphosphazobenzoyl obtained in this fashion was identical with the product synthesized from trichlorophosphazobenzoyl and sodium phenate; yield 32.7%.

Liquid (VI) was similarly prepared in 99.2% yield from p-nitrobenzoyl azide and triphenyl phosphite. It was identified by conversion to the diphenyl ester of p-nitrobenzoylamidophosphoric acid by boiling with 96% alcohol. Yield of diester 77.8%, m. p. 151-152°; it does not give a depression of melting point with the diester prepared from compound (VI) synthesized from trichlorophosphazo-p-nitrobenzoyl and sodium phenate.

SUMMARY

Triaroxyphosphazoacyls of the aromatic series and trimethoxyphosphazo-3,5-dinitrobenzoyl were prepared; some of their chemical properties were studied.

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* Original Russian pagination. See C. B. Translation.

NITROGEN COMPOUNDS OF PHENYLATED DERIVATIVES OF THIOPHENE. I.

V. N. Ivanova

Phenylated thiophenes, not to mention their nitrogen derivatives, form a very neglected branch of thiophene chemistry. The literature only contains short reports of the synthesis of a few phenylthiophenes [1]. Tetraphenylthiophene is an exception in that it has been studied in detail by Diltey and Graef [2].

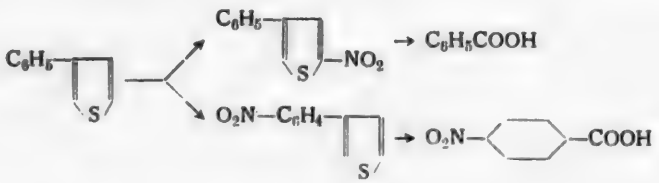
We chose monosubstituted α- and β-phenylthiophenes as compounds for study. They were synthesized by the method of A. S. Broun and M. G. Voronkov [3]. The nitration reaction was carried out in order to obtain nitrogen-containing derivatives of α- and β-phenylthiophenes. The usual methods of nitration did not give satisfactory results. Only when using copper nitrate as the nitrating agent in a medium of acetic anhydride (procedure of N. I. Putokhin [4]) did we observe a quiet course of the reaction with formation of nitro products in good yields (about 80%).

Nitration of β-phenylthiophene gave an adequately homogeneous crystalline product with a yellow color; m. p. 137-140°. The analysis corresponded to a mononitro compound of β-phenylthiophene.

Nitration of α-phenylthiophene led to two products. One of them (yield 75-80% of the total) consisted of golden-yellow crystals (needles) with m. p. 123-124°. The second nitro compound (yield 25-20%*) consisted of silvery yellow leaflets with m. p. 98-100°. In both cases the analyses corresponded to mononitro compounds of α-phenylthiophene.

It was necessary to elucidate the structure of these nitro compounds which had not been described in the literature. Oxidation was at first attempted with 5% potassium permanganate solution which was added in the theoretically calculated quantity. This procedure led, however, to complete decomposition of the molecule of the nitro compound (both the benzene and the thiophene rings broke down). More satisfactory oxidation conditions were established in a series of experiments. It was found necessary to introduce the oxidant in small portions and in low concentration (1% $KMnO_4$ solution) in quantity not exceeding 45-50% of the theoretical. Under these conditions the oxidation went very slowly and a proportion of the nitro compound (about 40%) was not oxidized.

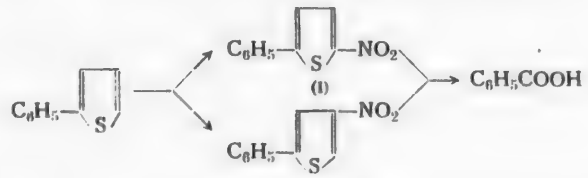
Oxidation of nitro-β-phenylthiophene gave two substances. One of these (about 70% of the total yield) was benzoic acid (identified by conversion to benzanilide). The second substance (about 30% of the total yield) was a finely crystalline powder with m. p. 237° (after sublimation). Judging by the analysis and melting point, the substance is p-nitrobenzoic acid. The isolation of two oxidation products – benzoic acid and p-nitrobenzoic acid – indicates that nitration of β-phenylthiophene goes in two directions:



The melting points of the two nitro compounds prepared from β-phenylthiophene are very similar. The other compound that did not undergo oxidation was found to be a nitro compound with the nitro group in the thiophene ring.

* As in original – Publisher's note.

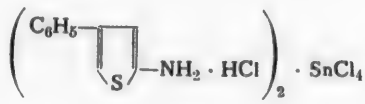
The structure of the nitro compounds of α-phenylthiophene was studied under the same conditions as for the nitro compounds of β-phenylthiophene. The product of oxidation of each of the two nitro derivatives of α-phenylthiophene was benzoic acid (identified as benzanilide). Nitration of α-phenylthiophene therefore also proceeds in two directions but in this case the nitro group always enters the thiophene ring. Taking into account the greater reactivity of the α-hydrogen atoms, the main product of nitration (m. p. 123-124°) must evidently be assigned the formula of α'-nitro-α-phenylthiophene (I). For the second product the formula of β'-nitro-α-phenylthiophene (II) is more probable. The transformations may therefore be represented as follows:



(I) (II)

The nitration reaction revealed a slight difference in the behavior of α- and β-phenylthiophenes. β-phenylthiophene gives a product with the nitro group in the benzene ring and one with the nitro group in the thiophene ring, whereas nitration of α-phenylthiophene gives substances with the nitro group only in the thiophene ring.

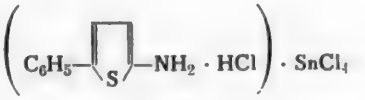
Reduction of the corresponding nitro compounds gave amino derivatives of α- and β-phenylthiophenes. The amines were isolated in the form of nicely crystallizing complex salts with tin chloride. Analysis of the complex salt of the amine prepared from a mixture of the nitro compounds of β-phenylthiophene corresponds to formula (A)



(A)

In proposing the above formula (A) we were guided by the fact that the formation of a complex salt with tin chloride is characteristic only of amines of thiophene but not of amines of benzene. We were unable to detect an amine in which the amino group was in the benzene ring. All attempts to isolate the free amine or its hydrochloride were unsuccessful, apparently due to the great instability of these substances.

Reduction of α'-nitro-α-phenylthiophene gave a complex salt of an amine with tin chloride whose analysis corresponds to formula (B)



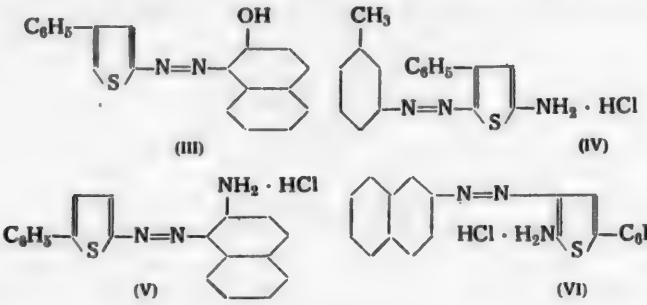
(B)

It was previously shown [5] that amines of thiophene in the form of their complex salts with tin chloride can be diazotized to give azo dyes. We also subjected the complexes of amines of α- and β-phenylthiophenes with tin salts to diazotization. Later it was shown that the diazo compounds from amines of α- and β-phenylthiophenes readily enter into the azo-coupling reaction with various aromatic amines, naphthols and their derivatives to form azo dyes. In this manner we obtained two dyes by coupling the diazotized complex salt of α'-amino-β-phenylthiophene in one case with β-naphthol (the dye forms dark-brown crystals) and in the other case with β-naphthylamine (brown, crystalline powder).

In addition we prepared dyes in which the azo component was the complex salt of α'-amino-β-phenylthiophene. In this case the yield of dye was considerably reduced. Again we obtained two dyes. Diazotized β-naphthylamine was coupled in one case with the complex salt of α'-amino-β-phenylthiophene (the resulting crystalline, cherry-red dye possessed indicator properties). In the other case diazotized m-toluidine was coupled

with the complex salt of α'-amino-β-phenylthiophene (the dye was dark-red; it satisfactorily dyed wool and silk but was less satisfactory on cotton).

In similar fashion α'-amino-α-phenylthiophene was the starting substance for two azo dyes: the first was obtained by coupling diazotized α'-amino-α-phenylthiophene with β-naphthylamine (brown crystalline dye); the second by coupling diazotized β-naphthylamine with the complex salt of α'-amino-α-phenylthiophene (the dye formed dark cherry-red crystals). The formulas of the prepared dyes are given below:



EXPERIMENTAL

I. Nitration of α-phenylthiophene. 2.25 g of copper nitrate and 15 ml of acetic anhydride were placed in a two-necked flask fitted with a thermometer extending to the bottom and a dropping funnel. The flask was cooled to 8-10° with iced water. A solution of 1.5 g of α-phenylthiophene in 15 ml of acetic anhydride was then run in portionwise from the dropping funnel. Addition of each portion caused the temperature to rise 2-4°. Nitration was performed at 10-12°. After the whole of the α-phenylthiophene solution had been added, the reaction mass was left at room temperature for 2 hours. The copper salts were then filtered under suction, and the filtrate was quickly treated with snow or crushed ice. This treatment caused an oil to separate which crystallized after 10-12 hours. Yield of crude nitro product 1.5 g.

The nitro product was recrystallized from hot 90% alcohol. On cooling, crystals came down in the form of golden needles with m. p. 121°; weight 0.825 g or 75% of the total yield of nitro compounds (substance 1); the crystals were quickly filtered.

More crystals came down from the mother liquor; these were silvery yellow leaflets, m. p. 95-97°, weight 0.275 g or 25% of the total yield (substance 2).

After recrystallization, substance 1 had m. p. 123-124°, and substance 2 had m. p. 98-100°.

Analysis of Substance 1

Found %: N 6.81 (Kjeldahl determination); S 15.80 (by oxidation with 5% $KMnO_4$). $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

Analysis of Substance 2

Found %: N 6.93; S 15.53. $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

II. Nitration of β-phenylthiophene. The procedure was similar to that with α-phenylthiophene. Reaction components were 1.8 g of copper nitrate in 10 ml of acetic anhydride, and 1.0 g of β-phenylthiophene in 10 ml of acetic anhydride. Yield of nitro derivative 0.8 g (62%). After recrystallization from 80% alcohol the product had m. p. 137-140°.

Found %: N 6.64; S 15.45. $C_{10}H_7O_2NS$. Calculated %: N 6.82; S 15.60.

III. Oxidation of nitro compounds of α- and β-phenylthiophenes. 1. Oxidation of nitro derivatives of β-phenylthiophene. 1 g of nitro compound and 100 ml of 1% potassium permanganate solution were placed in a 500 ml round-bottomed flask fitted with a reflux condenser. The flask was heated on a water bath. After 24 hours, the solution had lost its color; another 100 ml of 1% potassium permanganate solution was added, and

heating on the water bath was continued. After 4-5 days, the solution was again colorless. A final 100 ml of 1% potassium permanganate solution was added. In this manner, 50% of the theoretical quantity of potassium permanganate for complete oxidation of the thiophene had been added. After the solution had again become colorless, (9-days' heating on the water bath), the precipitated MnO_2 was filtered off, and the filtrate was evaporated and acidified with hydrochloric acid (d 1.19). A fine, heavy, cream-colored precipitate came down; m. p. 189-192°; weight 0.038 g (substance 1). The acid filtrate from substance 1 was evaporated; on cooling it deposited light, white crystals with m. p. 120°; weight 0.1 g (substance 2).

Substance 1 sublimes; after sublimation it has m. p. 237°. A qualitative test reveals absence of nitrogen.

Found %: N 8.26. $C_7H_5O_4N$. Calculated %: N 8.38.

Substance 2 readily sublimes. After sublimation it melts at 121-122°; it forms benzanilide with m. p. 158-159°. The substance is therefore benzoic acid.

2. Oxidation of nitro derivatives of α-phenylthiophene with m. p. 123-124° and m. p. 98-100° was performed in similar fashion to the above. Benzoic acid was isolated in both cases and identified as benzanilide with m. p. 158-160° and m. p. 158°.

IV. Reduction of nitro derivatives of α- and β-phenylthiophenes. 1. Reduction of α'-nitro-α-phenylthiophene. Into a 100 ml round-bottomed flask, equipped with a reflux condenser, were charged 0.8 g of the nitro derivative and 40 ml of tin chloride solution [16.2 g of $SnCl_2$, 57 ml of HCl (d 1.19) and 15 ml of H_2O]. After being heated on an air bath (60-70°) for 2 hours, the orange solution was decanted from the dark residue of unreacted nitro compound. A crumbly crystalline precipitate with a light-sandy color at once came down from the filtrate. Another 15 ml of the above solution of tin chloride was added to the residue in the flask, and the latter was again heated for 1-1.5 hours. The orange solution was again decanted from undissolved residue, and the latter was again treated with 10 ml of the tin chloride and again heated for about an hour. This operation was repeated once again. Light-sand colored crystals also came down from the decanted liquids. The four filtrates were combined and the product of reduction was filtered off; yield 0.7 g.

Found %: N 3.10; S 6.86; Sn 25.26 (by Kocheshkov's method). $(C_{10}H_7SNH_2 \cdot HCl) \cdot SnCl_4$. Calculated %: N 2.96; S 6.77; Sn 25.14.

2. Reduction of the nitro compound of β-phenylthiophene. 1 g of nitro compound and 50 ml of solution of stannous chloride in hydrochloric acid [16.2 g $SnCl_2$, 57 ml HCl (d 1.19) and 15 ml H_2O] were placed in a round-bottomed flask of 100 ml capacity. The flask (to which a reflux condenser was attached) was heated on an air bath without the contents being brought to the boil. Heating was continued until the whole of the nitro compound had gone into solution (small traces of blackened nitro compound remained), which usually occurred after 2-2.5 hours. The hot solution was filtered and the filtrate left in a cold place. Orange-red crystals of reduction product appeared at the bottom of the flask after 24 hours; m. p. 178-180° (in a sealed capillary).

Found %: N 3.95; S 9.24; Sn 17.21. $(C_{10}H_7SNH_2 \cdot HCl)_2 \cdot SnCl_4$. Calculated %: N 4.07; S 9.37; Sn 17.37.

V. Diazotization of the amines of α- and β-phenylthiophenes and preparation of azo dyes. 1. Diazotization of α'-amino-α-phenylthiophene. 0.2 g of the complex tin salt of α'-amino-α-phenylthiophene was dissolved by heating in alcohol; the solution was then cooled and 0.2 ml of HCl (d 1.19) was added. A solution of 0.04 g of $NaNO_2$ in 2-3 ml of water was run dropwise with constant stirring into the solution of the complex salt (cooled to 0-5°) at such a rate that the temperature did not rise above +5°. Completion of the diazotization reaction was indicated by the blue color of starch-iodide paper. After the $NaNO_2$ solution had been added, the diazo solution was kept for half an hour in an ice bath; after filtration, it was used for the azo-coupling reaction.

2. Preparation of azo dyes, derivatives of α'-amino-α-phenylthiophene. a) Diazo solution from 0.2 g of the complex salt of α'-amino-α-phenylthiophene (prepared as above) was gradually run with stirring and cooling (5-8°) into a hydrochloric acid solution of β-naphthylamine (0.07 g of β-naphthylamine was dissolved in 3-4 ml of alcohol by heating; after cooling, 0.3 ml of HCl, d 1.19, was added). The solution at first turned dark cherry-red; addition of saturated NaCl solution brought down a flaky, brown precipitate of dye (V). Yield 0.14 g.

Found %: S 8.58. $C_{20}H_{16}N_2SCl$. Calculated %: S 8.76.

b) 0.1 g of β-naphthylamine was dissolved in aqueous alcohol; 0.2-0.4 ml of HCl (d 1.19) was added. The solution was cooled to 3-5° and dropwise addition was made of $NaNO_2$ solution (0.03 g in 2 ml of water). The resulting diazo solution was filtered and run dropwise into a cooled alcoholic-acid solution of the complex salt of α'-amino-α-phenylthiophene (0.33 g of complex salt was dissolved in 3-4 ml of alcohol and 0.3 ml of HCl, d 1.19, was added). A dark cherry-red dye (VI) came down. Yield of dye 0.24 g.

Found %: S 8.60. $C_{20}H_{16}N_3SCl$. Calculated %: S 8.76.

3. Diazotization of α'-amino-β-phenylthiophene. 0.5 g of the complex salt of α'-amino-β-phenylthiophene was dissolved by heating in 5 ml of alcohol; to the stirred and cooled (0-5°) solution was gradually added (dropwise) a solution of $NaNO_2$ (0.112 g in 3 ml of water). The temperature was not allowed to rise above +5°. Development of a blue color on starch-iodide paper indicated the completion of diazotization. After filtration, the diazo solution was used for the azo-coupling reaction.

4. Preparation of azo dyes, derivatives of α'-amino-β-phenylthiophene. a) Diazo solution from 0.5 g of complex salt of α'-amino-β-phenylthiophene (for preparation see above) was gradually poured with stirring and cooling (5-8°) into an alkaline solution of β-naphthol (0.25 g of β-naphthol in 5 ml of 10% NaOH). The solution at first turned cherry to violet in color, and then deposited dye (III). Yield of dye 0.1 g.

Found %: S 8.94. $C_{20}H_{14}ON_2S$. Calculated %: S 9.09.

b) 0.33 g of m-toluidine was dissolved in 3 ml of alcohol; 1 ml of HCl (d 1.19) was added and the solution was cooled to 3-4°. A solution of 0.23 g $NaNO_2$ in 1.5 ml of water was added dropwise to the cooled solution. Completion of diazotization was indicated by the development of a blue color on starch-iodide paper. With constant stirring and cooling, the m-toluidine diazo solution was added dropwise to an acid-alcoholic solution of the complex salt of α'-amino-β-phenylthiophene (1 g of complex salt was dissolved in 15 ml of alcohol with heating; after it had cooled, 0.5 ml of HCl, d 1.19, was added). Azo-coupling goes very quickly; the solution becomes blood-red and dye (IV) rapidly comes down. Yield of dye 0.63 g.

Found %: N 12.54; S 9.81. $C_{17}O_{16}N_3SCl$. Calculated %: N 12.74; S 9.71.

In conclusion we extend our profound thanks to N. I. Putokhin for valuable advice.

SUMMARY

1. The nitration of α- and β-phenylthiophenes was studied. It was found that in both cases the reaction goes in two directions with formation of mononitro compounds. We synthesized α'-nitro-α-phenylthiophene, β'-nitro-α-phenylthiophene, α'-nitro-β-phenylthiophene, and (p-nitro-β-phenyl)-thiophene.

2. α'-Amino-α-phenylthiophene and α'-amino-β-phenylthiophene were synthesized in the form of complex salts with stannic chloride.

3. It was shown that in the form of complex salts with tin chloride, the amines of α- and β-phenylthiophenes can undergo diazotization and azo-coupling reactions, and can also be utilized as azo components.

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** In Russian.

THE ABSORPTION SPECTRA OF α- AND β-PHENYLTHIOPHENES AND THEIR NITRO DERIVATIVES. II

V. N. Ivanova

Methods of analysis based on molecular spectra are now widely used. Special attention has been paid to the regularities in the absorption spectra of organic compounds. It was found [1] that selective absorption in a specific region of the spectrum is often associated with the presence of a specific atomic grouping. When the same grouping is present in another molecule which may belong to an entirely different class of compounds, the same characteristic absorption is exhibited but disguised to some extent by the neighboring groups.

We made use of the data of molecular spectra in order to obtain a fuller characterization of the nitro compounds of α- and β-phenylthiophenes that we had prepared [2] and also in order to compare the absorption curves of the different nitro compounds. Absorption curves were plotted for the following substances: α- and β-phenylthiophenes, α'-nitro-α-phenylthiophene (m. p. 123-124°), β'-nitro-α-phenylthiophene (m. p. 98-100°), and mixtures of the isomeric nitro derivatives of β-phenylthiophene and α'-nitro-β-phenylthiophene.

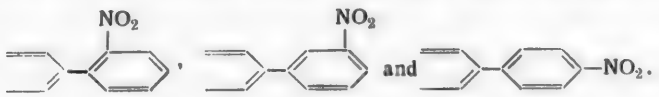
The curves of these compounds were compared with those of diphenyl and its mononitro derivatives. Comparison of the absorption curves of α- and β-phenylthiophenes with the absorption curve of their aromatic analog (diphenyl) leads to the conclusion that the general form of the absorption maxima of all of the three compounds is the same, but the replacement of benzene ring in diphenyl by a thiophene ring (in the formation of phenylthiophenes) causes the absorption maximum to be shifted towards longer wavelengths (Fig. 1). Diphenyl has λ_{max} 2470 A, β-phenylthiophene has λ_{max} 2600 A, while α-phenylthiophene has λ_{max} 2850 A. The last value illustrates the stronger effect of the benzene ring in the α-position on the shift of the absorption maximum.

Fig. 1. Absorption spectra of diphenyl (I), β-phenylthiophene (II) and α-phenylthiophene (III).

Fig. 2. Absorption spectra of o-nitrodiphenyl (I), m-nitrodiphenyl (II) and p-nitrodiphenyl (III).

Comparison of the absorption curves of o-, m- and p-nitro compounds of diphenyl reveals that the form of the curves varies in dependence on the position of the nitro group (Fig. 2).

Consequently in this case the absorption is caused by different atomic groupings, namely:



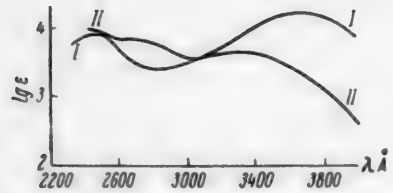


Fig. 3. Absorption spectra of α'-nitro-α-phenylthiophene (I) and β'-nitro-α-phenylthiophene (II).

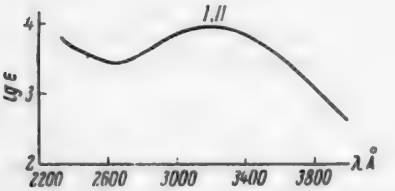
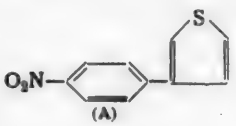


Fig. 4. Absorption spectra of a mixture of mononitro compounds of β-phenylthiophene (I) and α'-nitro-β-phenylthiophene (II). See text.

We observe a similar phenomenon on examination of the absorption curves of the isomeric nitro compounds of α-phenylthiophene (Fig. 3). There is no resemblance at all between the absorption curves of the two isomers. This is because the absorption is brought about by the nitro groupings in different positions (α- and β-) of the thiophene ring. A different picture is obtained when we plot the absorption spectra of nitro compounds of β-phenylthiophene. It was previously pointed out [2] that we had failed to separate the nitro compounds of β-phenylthiophene by crystallization. In one case the absorption measurements were made on an unresolved mixture of isomeric nitro compounds; in another case the sample was α'-nitro-β-phenylthiophene. It was found that both of the absorption curves have the same form and the same λ_{min} of 2650 A and λ_{max} of 3150-3200 A (Fig. 4). We can therefore conclude that one and the same substance is responsible for the spectral absorption curve in the two cases, namely α'-nitro-β-phenylthiophene. The absorption curve of the second substance in the mixture, present in insignificant quantity, could not be detected.



SUMMARY

1. Absorption curves of α- and β-phenylthiophenes were plotted and found to be similar to the absorption curve of diphenyl.

2. The absorption spectra of α'-nitro-α-phenylthiophene, β'-nitro-α-phenylthiophene and α'-nitro-β-phenylthiophene were plotted.

The absorption spectra were obtained in the laboratory of the chemical faculty of Moscow State University.

In conclusion it is our duty to express our gratitude to L. A. Kazitsyna for assistance in the plotting of the absorption spectra.

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Kuibyshev Industrial Institute

THE ABSORPTION SPECTRA AND STRUCTURE OF SUBSTITUTED QUINOLINES SERVING AS STARTING SUBSTANCES FOR ANTIMALARIALS

V. STRUCTURE AND TAUTOMERISM OF THE 2- AND 4-AMINOQUINOLINES

V. I. Blizniukov and N. T. Solonskaia

Spectroscopic methods are undoubtedly valuable for clarification of the structure and tautomerism of 2- and 4-aminoquinolines, although the conclusions from different investigations are not always consistent. Steck and Ewing [1], for example, and Hearn, Morton and Simpson [2] consider these compounds to be tautomeric on the basis of a study of the ultraviolet spectra, whereas the spectral data of Angual and Werner [3] indicate the absence of tautomerism. A closer study of the spectrography of 2- and 4-aminoquinolines was carried out in the present work in solutions of hexane, ethanol, dioxane, chloroform and water, as well as in solutions of perchloric, sulfuric and hydrochloric acids and in alkaline solutions of sodium ethoxide. The compounds were investigated in the concentration range of $2 \cdot 10^{-2}$ to $2 \cdot 10^{-5}$ molar.

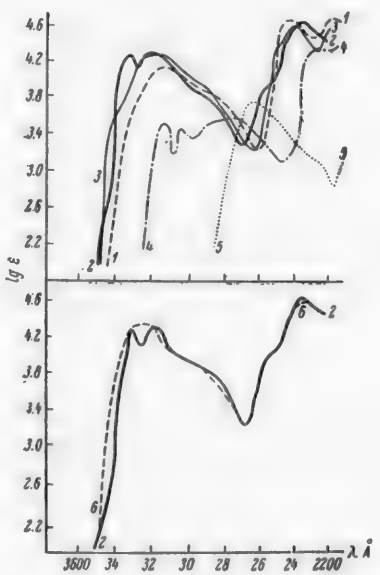


Fig. 1. Absorption spectra. 1) 4-aminoquinoline in dioxane; 2) 4-aminoquinoline in water; 3) 4-aminoquinoline in ethanol; 4) quinoline in ethanol; 5) 4-aminoquinoline in water (the spectrum is one tenth as intense); 6) 1-methyl-4-iminoquinoline in water.

2-Aminoquinoline was prepared by the action of sodium amide on quinoline [4] (m. p. 130°), while 4-aminoquinoline was prepared by the action of ammonia on 4-chloroquinoline in fused phenol in similar fashion to the preparation of 4-amino-7-chloroquinoline [5] or Akrikhin* [6], m. p. 155°. 1-Methyl-4-iminoquinoline was obtained by V. I. Konovalov from 4-aminoquinoline in a manner similar to the preparation of 10-methyl-9-iminoacridine [7,8]; it had m. p. 134° (with decomp.). 4-Acetylaminoquinoline was prepared by acetylation of 4-aminoquinoline with acetic anhydride [7]; m. p. 176°. Before use, the purified 2- and 4-aminoquinolines were recrystallized from benzene, the 1-methyl-4-iminoquinoline was recrystallized from absolute ether, and the 4-acetylaminoquinoline from ethanol.

According to [1] 4-aminoquinoline has three absorption bands in ethanol; according to [2] it has two bands. We found five bands in solutions in ethanol, dioxane and water.

According to [1] 2-aminoquinoline has two absorption bands in ethanol and alkali solution. We detected three absorption bands in solutions in ethanol, hexane, dioxane and chloroform.

In general appearance and arrangement, the bands of 2- and 4-aminoquinolines in organic solvents are similar to the spectra of unsubstituted quinoline. The bands of the latter are characteristic of benzene and pyridine (Fig. 1, curves 1-4 and Fig. 5, curves 1-5). This signifies that in molecules of aminoquinolines the benzene and aminopyridine rings interact in the same manner as the benzene and pyridine rings

* Transliteration of Russian — Publisher's note.

interact in unsubstituted quinoline [9,10]. On the basis of this similarity, we arbitrarily speak of the "benzene" and "pyridine" absorption bands of the isomeric aminoquinolines.

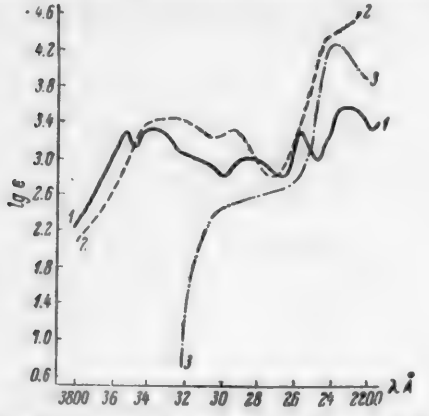


Fig. 2. Absorption spectra. 1) 1-methyl-4-iminoquinoline in hexane; 2) 1,4-naphthoquinone in absolute ethanol [25]; 3) 1,4-benzoquinone in hexane [26].

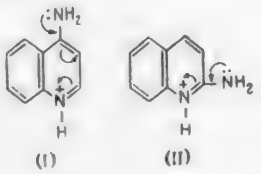
Under the influence of ionizing solvents such as water, or on formation of a salt at the ring nitrogen, a fourth band appears in the absorption spectra in the form of an inflection with λ_{max} 2580 A and ϵ 50,000; at the same time the fine structure of the long-wave benzene band of 4-aminoquinoline becomes conspicuous (Fig. 1, curves 2 and 5; Fig. 3, curves 1-3). The band with λ_{max} 2580 A becomes stronger in the spectrum of the 4-acetylaminoquinoline ion (Fig. 3, curves 4 and 7). Judging by its origin, the band with λ_{max} 2580 A must be included among the bands formed by the conjugation of the NH_2 group with the ring and the ring nitrogen, just as in the case of 4-aminopyridine. For this reason the band in question is called the "p-aminopyridine" absorption band, but it is one tenth as strong as the corresponding band of 4-aminopyridine.

The spectra of the aqueous solution of 2-aminoquinoline or of its ion exhibit "o-aminopyridine" absorption bands of nearly the same intensity as the bands of 2-aminopyridine, which are superposed on the "benzene" spectrum of 2-aminoquinoline (Fig. 5, curves 3, 6, 7; Fig. 6, curves 1-4).

The influence of the amino group on the quinoline system in molecules of 2- and 4-aminoquinolines is reflected in activation of the benzene ring and in deactivation of the pyridine ring. Indirect proof of this is the increased intensity of their "benzene" absorption bands and weakened intensity of the aminopyridine absorption bands in comparison with the corresponding bands of quinoline or 2- and 4-aminopyridines (Fig. 1, curves 3-5 and Fig. 5, curves 3 and 7).

The absence of "aminopyridine" bands from the spectra of 2- and 4-aminoquinolines dissolved in non-ionized solvents can be accounted for by association of molecules. These conclusions were supported by molecular weight determinations. The degree of association of 4-aminoquinoline was found to be considerably higher than that of 2-aminoquinoline. Even in solutions of the order of 10^{-3} molar, the association of 2- and 4-aminoquinolines does not disappear entirely. Indirect proof of this is the appearance of "o-aminopyridine" bands in the spectrum of the hexane-water solution of 2-aminoquinoline. Presumably the small quantity of water (0.07%) dissolved in the hexane dissociates the less associated molecules of 2-aminoquinoline but to a considerably smaller extent than in the case of 2-aminopyridine [11].

The associated molecules are dissociated under the influence of ionizing solvents such as water or on formation of a salt at the ring nitrogen, a positive charge being developed at the latter. This leads to rearrangement of the electronic density along the amino group toward the positively charged ring nitrogen. Conjugation is set up between the amino group, the π-electrons of the pyridine ring and the ring nitrogen (electron-accepting), just as in the cases of 2- and 4-aminopyridines [11] (I and II).



(I) (II)

This interpretation is confirmed by the increased basicity of the ring nitrogen of 4-aminoquinoline in comparison with the basicity of quinoline [11].

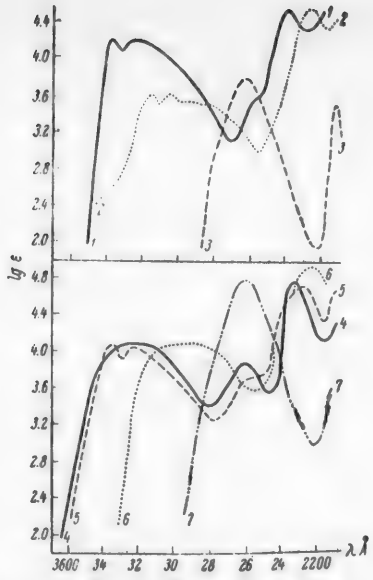


Fig. 3. Absorption spectra. 1) 4-aminoquinoline in ethanolic HCl (molar ratio 1:100); 2) 4-chloroquinoline in ethanolic HCl (molar ratio 1:100); 3) 4-aminopyridine in ethanolic HCl (molar ratio 1:100); 4) 4-acetylaminoquinoline in ethanolic HCl (molar ratio 1:100); 5) 4-acetylaminoquinoline in 5 M ethanolic HCl (after 30-minutes' heating on water bath); 6) 4-acetylaminoquinoline in neutral ethanol; 7) 4-aminopyridine in ethanolic HCl.

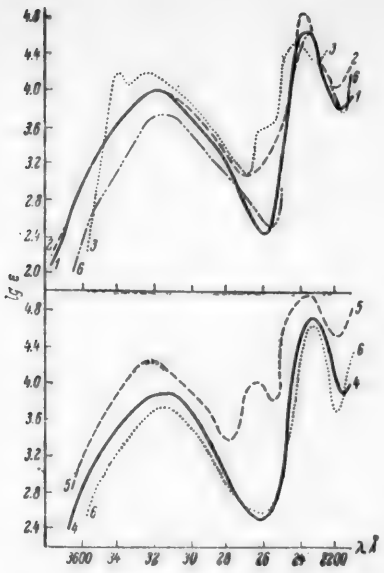


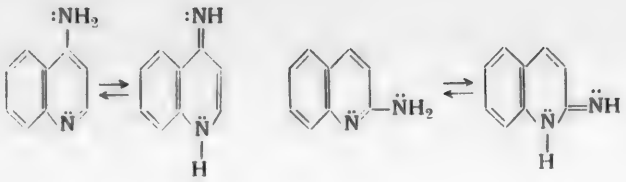
Fig. 4. Absorption spectra. 1) 4-aminoquinoline in concentrated sulfuric acid; 2) 4-aminoquinoline in 12 M perchloric acid; 3) 4-aminoquinoline in ethanolic HCl (molar ratio 1:100); 4) 4-acetylaminoquinoline in concentrated sulfuric acid; 5) 4-acetylaminoquinoline in 12 M perchloric acid; 6) quinoline in concentrated sulfuric acid.

The structure of the singly-charged 4-aminoquinoline ion has been frequently discussed [12-15]. None of the speculations about the addition of a proton to the ring nitrogen take into account, however, the possibility of interaction of the benzene ring with the aminopyridine ring and of conjugation of the amino group with the ring and the ring nitrogen.

Formation of a salt at the amino group and simultaneously at the ring nitrogen results in disappearance of the influence of these groups on the pyridine ring. The spectra of 2- and 4-aminoquinolines in concentrated sulfuric acid then become similar to the spectra of the unsubstituted quinolinium ion (Fig. 4, curves 1, 4, 6 and Fig. 6, curves 5 and 6). In solution in a weaker acid, however, such as 12 M perchloric acid, salt formation at the amino group of 4-aminoquinoline and 4-acetylaminoquinoline is incomplete, and a corresponding equilibrium is established between their singly-charged and doubly-charged ions (Fig. 4, curves 2, 5 and 6).

Absence of sulfonation on dissolution of 2- and 4-aminoquinolines in concentrated sulfuric acid was proved by observation of the spectra plotted after the sulfuric acid solutions had been diluted 5-fold (20% H_2SO_4 content). The resulting curves were identical with those obtained for a solution in 5 M ethanolic hydrogen chloride. No process other than salt formation therefore takes place in concentrated sulfuric acid.

The isomeric 2- and 4-aminoquinolines, which resemble the corresponding compounds of the pyridine series, are markedly different in chemical properties from their isomers in which the amino group is in position 3 of the pyridine ring or in the benzene ring. Thus, for example, 2- and 4-aminoquinolines are not diazotized under normal conditions [16-20]; they form two series of derivatives with alkyl halides [21, 22]; they do not give salts with 2 equivalents of hydrogen chloride, and they are the strongest bases [12]. The dual reactivity of 2- and 4-aminoquinolines and their other [23-25] special characteristics have been explained by tautomerism between the amino and imino forms:



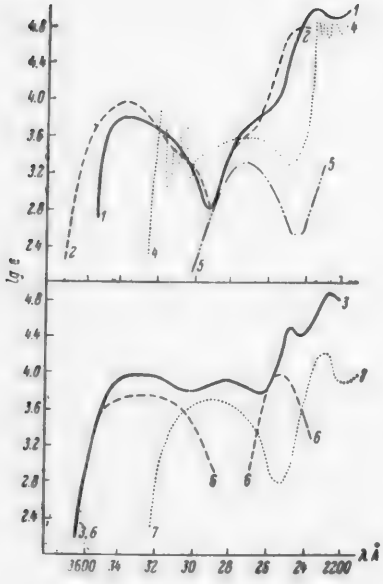


Fig. 5. Absorption spectra. 1) 2-aminoquinoline in hexane; 2) 2-aminoquinoline in ethanol; 3) 2-aminoquinoline in water; 4) 2-chloroquinoline in hexane; 5) pyridine in hexane (spectrum displaced 200 A toward the long waves); 6) 2-hydroxyacetophenone in ethanol [33]; 7) 2-aminopyridine in water.

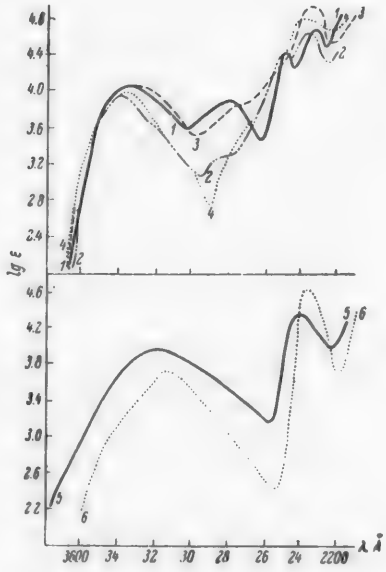
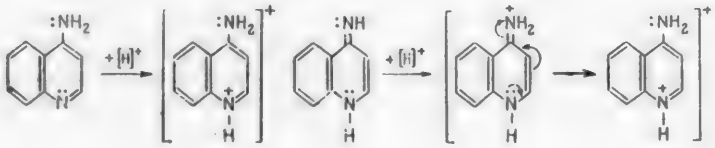


Fig. 6. Absorption spectra. 1) 2-aminoquinoline in ethanolic HCl (molar ratio 1:100); 2) 2-aminoquinoline in ethanolic HCl (molar ratio 1:0.1); 3) 2-aminoquinoline in ethanolic HCl (molar ratio 1:1); 4) 2-aminoquinoline in ethanol; 5) 2-aminoquinoline in concentrated sulfuric acid; 6) quinoline in concentrated sulfuric acid.

It is true that the spectrum of 4-aminoquinoline is hardly shifted when salt formation takes place at the ring nitrogen, in contrast to what happens in the case of 3-aminoquinoline. Moreover, 1-methyl-4-iminoquinoline gives a spectrum in water and in acid solutions which is identical with the spectrum of the 4-aminoquinolinium ion (Fig. 1, curves 6 and 2). This similarity between the absorption spectra of 4-aminoquinoline and 1-methyl-4-iminoquinoline could also have arisen if they had different structures but on condition that in the former (the amino form) the salt-forming center was the ring nitrogen, and that in the latter (the imino form) the salt-forming center was the nitrogen of the imino group.



In both cases the same 4-aminoquinolinium ion is formed, and this also governs the identity of the spectra of the two substances both in an acid medium and in ionizing solvents. In anhydrous hexane or dioxane, which do not bind the unshared electron pair of the nitrogen of the 4-imino group or of the ring nitrogen, the spectrum of 1-methyl-4-iminoquinoline has nothing in common with the spectrum of 4-aminoquinoline (Fig. 1, curve 2 and Fig. 2, curve 1).

We attempted to explain the origin of the absorption bands in the spectrum of 1-methyl-4-iminoquinoline by comparing it with the spectra of 1,4-naphthoquinone and 1,4-benzoquinone in hexane. The comparison (Fig. 2, curves 1 and 2) revealed a satisfactory similarity. Superposed on the "quinone-imine" spectrum of 1-methyl-4-iminoquinoline with three bands, as in the case of 1,4-benzoquinone [27], are the "benzene" bands as in the case of naphthoquinone or 4-aminoquinoline. This could only happen if the pyridine ring was lacking in aromatic character.

As a model of the tautomeric amino form we took 4-dimethylaminoquinoline; according to the literature [1] the spectrum of the latter resembles that of 4-aminoquinoline but not that of 1-methyl-4-iminoquinoline, when examined both in organic solvents and in acidic and alkaline solutions.

The amino structure of 4-aminoquinoline is also confirmed by measurements of its dipole moment [28] (μ 4.4 D), which is considerably higher than the dipole moment of quinoline [29] (μ 2.18 D).

With the objective of detecting the two hypothetical tautomeric forms, we studied the absorption spectra of 2- and 4-aminoquinolines in a large number of organic solvents and in acid and alkaline media, both immediately and after the passage of a few days after preparation of the solutions. If a tautomeric equilibrium had been established, we should expect to find the "benzene-quinoneimine" bands (of the imino form) superposed on the "benzene-aminopyridine" bands (of the amino form), but no evidence of this could be found on careful examination. Changes took place in the absorption spectra of 2- and 4-aminoquinolines in acid solutions when the quantity of acid was more than 5-10 moles per mole of these compounds. These can be correlated with the usual reactions of salt formations at the ring nitrogen, and are not due to tautomeric transformations.

It has been noted [30] that the existence of heterocyclic amines in the amino form is caused by displacement of the amino-imino equilibrium towards the side of the amino form to the extent to which the basicity constant of the imino form exceeds the basicity constant of the amino form. A concentration of the imino form in solutions which is not detectable by the spectral method nevertheless does not exclude the possibility of a reaction involving tautomeric transformation of the amino form into the imino form. At the same time we can accept the views of A. N. Nesmeianov [31, 32] and explain the dual reactivity of 2- and 4-aminoquinolines by conjugation of groups and transfer of the reactive center from the ring nitrogen to the amino group, and conversely in dependence upon the reaction conditions and the influence of the reagent used.

SUMMARY

1. The influence of solvents and of acid and alkaline solutions on the absorption spectra of 2- and 4-aminoquinolines, 4-acetylaminoquinoline and 1-methyl-4-iminoquinoline was studied.

2. It was established that in solvents with little effect on the ring nitrogen (hexane, dioxane), the "benzene-pyridine" spectrum predominates in the case of 2- and 4-aminoquinolines, and the "benzene-quinoneimine" spectrum in the case of 1-methyl-4-iminoquinoline.

3. It was established that under the influence of ionizing solvents and hydrochloric acid of various concentrations the "benzene-pyridine" spectrum of 2- and 4-aminoquinolines remains substantially unaltered, but "o- or p-aminopyridine" bands are developed which indicate conjugation of the positively charged ring nitrogen with the ring and with the 2- or 4-amino group.

4. It was shown that formation of the doubly-charged ions of 2- and 4-aminoquinolines in concentrated sulfuric acid is accompanied by reversion to the spectrum of the unsubstituted quinolinium ion.

5. The ultraviolet absorption spectra of 2- and 4-aminoquinolines indicate the absence of tautomerism of these compounds.

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THE ABSORPTION SPECTRA AND STRUCTURE OF ACRIDINE

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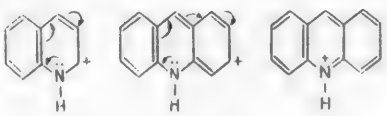
Many studies have been made [1-4] of the spectrography of acridine. We studied the absorption spectra of acridine in ethanol, dioxane, carbon tetrachloride, dichloroethane, ethanolic hydrochloric acid of various concentrations, 98% sulfuric acid, and 60% perchloric acid at concentrations of 10^{-3} to 10^{-5} molar.

The absorption spectrum of acridine has the general character of the quinoline spectrum [5], but under the influence of the condensed benzene ring it is very much displaced toward longer waves in comparison with the quinoline spectrum. Thus, the long-wave band of acridine is bathochromically displaced by about 400 A, and the short-wave band by 200-300 A (Fig. 1, curves 1, 2; compare 3; curves 4 and 5, compare 6). In addition the long-wave band is 3-5 times more intense and the short-wave bands 5-8 times more intense than the quinoline bands. Due to this heightened intensity of the bands, arbitrarily called "benzene" bands, the "pyridine" band of acridine with λ_{max} 3100 A and ϵ 2500, is covered by the edge of the long-wave "benzene" band, and therefore in the spectrum of acridine in solution in dioxane or hexane the "pyridine" band is not sharp (Fig. 1, curves 2, 4, compare with 3 and 6). The sharper "pyridine" band of acridine with a fine structure is detected in the spectrum of 9-aminoacridine in hydrochloric acid solution (Fig. 1, curve 7).

Formation of an acridine salt is accompanied by a bathochromic shift of the long-wave edge of the acridine band by 200 A and by a relatively small bathochromic shift of the edge of its short-wave band. A broad absorption band with λ_{max} 3980 A and ϵ 3200 is formed at the start of the visible region (Fig. 2, curves 1-3). In form and position this band can be classed with the "ortho type" of benzene bands [6]. The other short-wave band of the "ortho type," with an orientatory maximum at λ 2500-2600 A is not observed in the spectrum of the acridine salt, since presumably it falls into the region of absorption of the stronger short-wave "benzene" band of acridine which is approximately in the same region. A short-wave band of the "ortho type" is observed in the spectrum of the salt of 9-acetyl-aminoacridine (see Fig. 2, curve 5).

Judging by the nature of the absorption, the spectrum of the acridinium ion is a complex one; it consists of "benzene" bands, as in anthracene, on which are superposed "benzene" bands of the "ortho type" (Fig. 2, curves 6, 7, 8 and 10). The same bands of the "ortho type" are found in the spectrum of the quinolinium ion, but in the case of the acridinium ion they are considerably shifted toward the visible region just as in the case of the ion of 6-aminoquinoline (Fig. 2, curve 9).

The development of "benzene" bands of the "ortho type" in the spectrum of the acridinium ion is evidently due to the ability of the positive charge in the acridinium ion to move from the ring nitrogen to the carbon atom in the 3 (6) position (formula II), just as the positive charge of the quinolinium ion can move from the ring nitrogen to the second carbon atom [5] (formula I).



(I) (II) (III)

The presence of the "benzene" absorption bands of the same type as in anthracene may indicate, however, that the aromatic system of the pyridine ring with a positive charge at the ring nitrogen is retained intact in the acridinium ion (formula III).

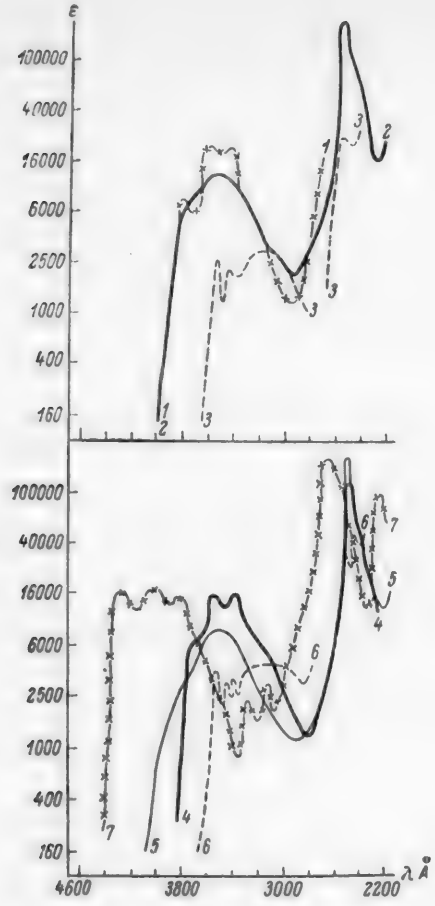


Fig. 1. Absorption spectra. 1) Acridine in CCl_4; 2) acridine in dioxane; 3) quinoline in ethanol [5] (the long-wave branch of the curve is bathochromically displaced by 400 A, and the short-wave band is displaced by 300 A); 4) acridine in hexane; 5) acridine in ethanol; 6) quinoline in hexane [5] (the long-wave branch of the curve is bathochromically displaced by 400 A, and the short-wave branch by 200 A); 7) 9-aminoacridine in standard HCl solution (molar ratio 1:1).

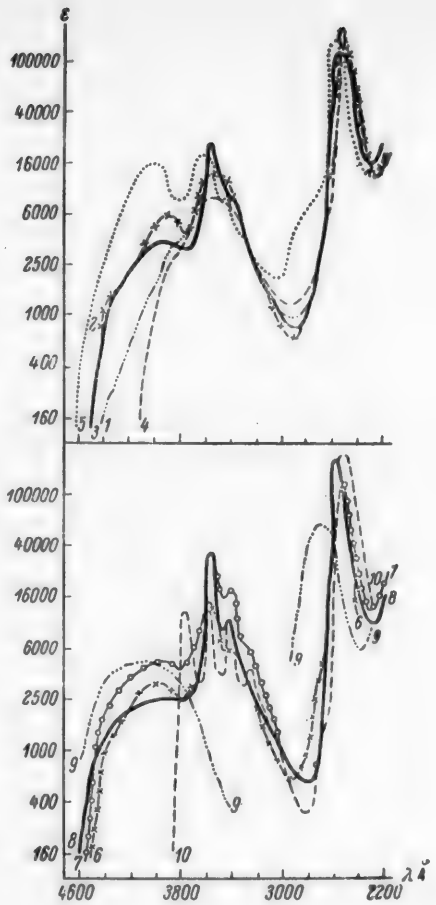


Fig. 2. Absorption spectra. 1) Acridine in standard HCl solution (molar ratio 1:0.2); 2) acridine in standard HCl solution (molar ratio 1:1); 3) acridine in standard HCl solution (molar ratio 1:100); 4) acridine in ethanol; 5) 9-acetyl-9-aminoacridine in 60% $HClO_4$; 6) acridine in 5 M ethanolic HCl; 7) acridine in 60% $HClO_4$; 8) acridine in concentrated H_2SO_4; 9) 6-aminoquinolinium ion (part of curve); 10) anthracene in hexane.

These data from the spectrographic investigation, which demonstrate the weakening of the aromatic character of the pyridine ring of acridine after salt formation, are in harmony with oxidation data. Thus, the acridinium ion is oxidized at the pyridine ring with formation of acridone [7]. On the other hand, the oxidation of acridine in an alkaline medium easily leads to rupture of the benzene ring with formation of quinoline-2,3-dicarboxylic acid [8].

SUMMARY

1. Acridine in organic solvents gives a complex ultraviolet absorption spectrum containing bands characteristic of the pyridine (quinoline) ring and benzene. The reciprocal influence of the rings is reflected in a

heightening of intensity and in a shift of the respective absorption bands toward the long-wave region.

2. The absorption spectrum of the acridinium ion in acid solutions is regarded as a complex spectrum comprising the benzene bands of "anthracene" and benzene bands of the "ortho type" which are superposed.

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RELATION BETWEEN THE ACIDITY OF ACYCLIC POLYOLS AND THE LENGTH OF THE POLYHYDROXYMETHYLENE CHAIN

L. A. Mai

The acidity of acyclic polyols (polyhydric alcohols) depends in great measure on the length of the polyhydroxymethylene chain [1]. We established that the relation between the dissociation constants (K) of polyols of the structure $HOCH_2(CHOH)_nCH_2OH$ and the number of CHOH groups (n) can be expressed by the following formula when n is 0, 1, 2 or 4:

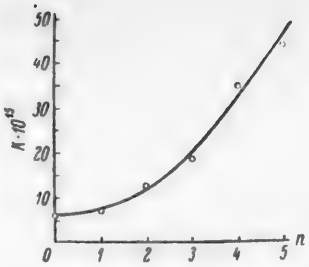
$$K(n) = a + bn^c,$$
$$\text{where } a = 6 \cdot 10^{-15},\ b = 1 \cdot 10^{-14},\ c = 2.3. \qquad (1)$$

In order to check this interesting functional dependence we determined the acidity constants of xylitol (n = 3) and D-gluco-D-guloheptitol (n = 5) by an approximate electrometric method. The values are in good agreement with those calculated from equation (1) (see table).

n	Compound	pK found from expt.	pK from equation (1)
0	Ethylene glycol	14.24 [1]	14.22
1	Glycerine	14.16 [1]	14.16
2	Meso-erythritol	13.90 [1]	13.96
3	Xylitol	13.73	13.73
4	Dulcitol	13.46 [1]	13.52
5	D-gluco-D-guloheptitol	13.35	13.33

We also determined the acidity constant of D-mannitol in order to confirm the absence of error that could have crept in on comparison of the values of Michaelis (1913) [1] for the acidity constants of polyols with n = 0, 1, 2 and 4 with our own data for polyols with n = 3 and 5. The difference between our value ($K = 3.80 \times 10^{-14}$, pK = 13.42) and the value found by Michaelis ($K = 3.4 \times 10^{-14}$, pK = 13.47) lies within the limits of error of measurement. An error of between ± 0.05 and 0.1 pH must be assumed in measurements of pH in the vicinity of 14 with the hydrogen electrode, due to the indeterminate character of the diffusion potential, the low degree of buffering of the solutions, and other factors.

The acidity of the acyclic polyols therefore appreciably increases with the length of the polyhydroxymethylene chain, at least up to the hexitols-heptitols. Due to the absence of data for octitols and nonitols it is impossible at present to predict the character of the further change of acidity with chain length; it is highly probable that with increasing number of CHOH groups between the CH_2OH groups beyond 5, the acidity will gradually approach an asymptotic value (see diagram).



Acidity constant K of polyols $HOCH_2(CHOH)_nCH_2OH$ as a function of the number of CHOH groups (n).

EXPERIMENTAL

Xylitol was prepared from D-xylose by reduction with sodium amalgam [2]: a colorless, non-crystallizing syrup; m. p. of the dibenzal derivative 172-174°. D-Gluco-D-guloheptitol was prepared from D-gluco-D-guloheptonolactone by reduction with sodium amalgam [3] and was recrystallized from methanol; m. p. 126-127°.

CO_2-free double-distilled water and CO_2-free alkali were used in the measurements which were performed with a hydrogen electrode at 18°. The measuring cell comprised $Pt-PtO_2-H_2$ | solution of polyol and its salt | saturated KCl solution | saturated calomel electrode. The ionic strength of the solutions was 0.01; the concentration of the polyol was 0.5 M and that of the NaOH 0.01 M. The mean of three independent measurements was taken. The error of measurement was ±0.05-0.1 pH.

SUMMARY

1. The acidity constants of xylitol, D-mannitol and D-gluco-D-guloheptitol were determined by an approximate electrometric method.

2. The acidity of the acyclic polyols increases with the chain length, at least as far as the hexitols–heptitols.

3. A functional relation between dissociation constants of acyclic polyols and chain length was found, in good agreement with the experimental data.

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THE ACIDITY OF SOME MONOSUBSTITUTED ACETIC ACIDS AND THE ELECTRONIC AFFINITY OF SUBSTITUENTS

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The increased acidity of polar-substituted acetic acids in comparison with acetic acid itself is known to be due to the electrostatic effect of the substituting atom or atomic group. The functional relation between the magnitude of the acidity constant of monosubstituted acetic acids and the nature of the substituent is of interest for the study of the reciprocal influence of atoms in such molecules.

It has been suggested that the change in acidity of monohalosubstituted acetic acids (ΔpK) due to a polar substituent is exclusively a field effect:

$$\frac{\Delta pK}{E} = \text{const},$$

where E is the dipole field [1]. However, the most recent values of pK of monohalosubstituted acetic acids, obtained by very accurate conductometric measurements [2], do not reveal very good constancy of the $\Delta pK/E$ ratio; in addition to the field effect (if this is involved) an other electrostatic factor must evidently come into play: the polarizability of the halogen–carbon bond [2].

Dissociation Constants of Some Monosubstituted Acetic Acids and the Electronic Density of the Substituents

Substituent	$-\log K$	E (ev) [3]	$-E \log K$
F	2.59	4.03	10.44
Cl	2.87	3.74	10.73
Br	2.90	3.65	10.58
I	3.17	3.30	10.46
CN	2.47	3.60	8.89
OH	3.83	2.16	8.27
SH	3.54	2.60	9.20

We established that for monohalosubstituted acetic acids as well as for cyanoacetic, mercaptoacetic and glycolic acids there is a reciprocal proportionality between the energy of acid dissociation (energy expended on removal of a proton from the COOH group) and the electronic affinity of the substituent (energy expended on removal of an electron from the corresponding anion); the energy of the reaction

$$XCH_2COO^- + H^+ \rightarrow XCH_2COOH$$

is inversely proportional to the energy of capture of an electron by the substituting atom or group $X + e^- \rightarrow X^-$, i.e., $-E \log K = \text{const}$, or $K^E = \text{const}$., where E is the electronic affinity of the given atom or atomic group. For halogens $-E \log K = 10.55$ ev, and $K^E = 2.818 \times 10^{-11}$; for OH-, SH- and CN-substituted acetic acids, these constants are respectively 8.79 ev, and 1.622×10^{-9}. For halo-substituted acetic acids the deviation of the value of $-E \log K$ from the mean does not exceed ± 0.18. The value of $-E \log K$ varies rather more in the cases of

OH-, SH- and CN-substituted acetic acids (see table); the deviations of 0.52 are evidently due not only to the inaccuracy of the corresponding values of the dissociation constants and electronic affinity but mainly to other factors that influence the dissociation of these acids and that are associated with the more complex structure of the substituting groups; for example the presence of a second ionizable H atom at the O and S atoms in mercaptoacetic and glycolic acids and the possibility of formation of a cyclic structure through a hydrogen bond. In cyanoacetic acid a part is played by the dipole $\overline{N}=\overset{+}{C}$.*

The value of the product $-E\log K$ for acetic acid (3.38) is very different from the constants listed above; this may be associated with the unique electronic structure of the hydrogen atom which prevents comparison with halogen atoms.

The relatively good constancy of $-E\log K$ for monohalosubstituted and also (as we must assume) for other monosubstituted acetic acids may provide an opportunity for determining (or at least for evaluating) the electron affinity of some atoms and atomic groups such as astatine (halogen 85), SeH, TeH, SCN, $\overset{+}{N}H_3$, etc., independently of methods known at the present time (energy of the crystalline, ionic lattice with the help of the Haber-Born cycle, the space charge, the absorption spectra, the minimum electron-acceleration voltages for ionization of gases, or extrapolation from the isoelectronic series).

The relation in question of course does not allow conclusions to be reached about the mechanism of the reciprocal influence of a substituent and the protonizable H atom of the COOH group. In the case of halogen substituents, however, the most probable mechanism is a shift of electronic density from atom to atom along a chain of covalent bonds; this mechanism is supported by the marked inverse proportionality of the energy of dissociation and the electron affinity of a halogen which characterizes the tendency to complete the octet.

SUMMARY

The dissociation constants of monohalosubstituted acetic acids are inversely proportional to the magnitudes of the electronic affinities of the halogen. The same relation also applies to cyanoacetic, glycolic and thioglycolic acids, but the latter have a different value of the constant $-E\log K$.

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* It is interesting to note that the dissociation constants of cyanoacetic acid (2.47) and glycine for $H_3\overset{+}{N}CH_2COOH \rightleftharpoons H^+ + H_2NCH_2COOH$ (2.40) are very similar.

SYNTHESIS AND TRANSFORMATIONS OF SUBSTITUTED VINYL ETHERS

VI. SYNTHESIS OF α-METHYLVINYL ARYL AND α-METHYLVINYL CYCLOHEXYL ETHERS

M. F. Shostakovskii, E. P. Gracheva and N. K. Kul'bovskaia

α-Methylvinyl aryl ethers have not been extensively studied. Two methods for their preparation have been described. Ruhemann and Wragg [1] synthesized α-methylvinyl phenyl ether by the reactions

$$CH_3-\underset{\displaystyle Cl}{\underset{|}{C}}=CH-COOC_2H_5 + C_6H_5ONa \xrightarrow{t} CH_3-\underset{\displaystyle OC_6H_5}{\underset{|}{C}}=CHCOOC_2H_5 \longrightarrow$$

$$\longrightarrow CH_3-\underset{\displaystyle OC_6H_5}{\underset{|}{C}}=CH-COOH \xrightarrow{-CO_2} CH_3-\underset{\displaystyle OC_6H_5}{\underset{|}{C}}=CH_2$$

The efficiency of the method is not, however, stated in the paper.

Niederl and Storch [2] isolated the phenyl and cresyl ethers by the action of isopropenyl bromide on the corresponding potassium phenoxide.

$$CH_3-\underset{\displaystyle Br}{\underset{|}{C}}=CH_2 + ArOK \xrightarrow{t} CH_3-\underset{\displaystyle OAr}{\underset{|}{C}}=CH_2$$

This reaction is limited mainly by the poor availability of isopropenyl bromide and by the low yield of the ether.

In the present work we studied the conditions of synthesis of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers by the method of Favorskii and Shostakovskii.

$$CH_3-C\equiv CH + HOAr \xrightarrow[200-220^\circ]{KOH} CH_2=\underset{\displaystyle CH_3}{\underset{|}{C}}-OAr$$

The employment of propyne as the vinylating agent leads to a lower yield in comparison with the vinylation of phenols with acetylene [3, 4]. This method is nevertheless more convenient than any of the existing methods of preparation of α-methylvinyl aryl ethers. A study of the conditions for this synthesis established that partial prevention of resinification and improvement of the yields of α-ethers necessitates the use of 1 mole of potassium hydroxide per mole of phenol and an excess of propyne (Table 1).

In all cases, however, a considerable amount of resin is obtained; its nature will be investigated later.

We undertook a study of the effect of propadiene in this reaction. Propadiene is present in the original mixture [5] and is formed by isomerization

$$CH_3C\equiv CH \rightleftarrows CH_2=C=CH_2$$

TABLE 1

Substance vinylated (1 mole)	Quantity of KOH in the form of 66% aqueous solution (moles)	Quantity of propyne (moles)	Reaction temperature	Duration of experiment (hours)	% yield
Phenol	1	2	220°	4	40
Phenol	0.3	2	220	9	5
Phenol	1	2	220	2	10
Phenol	1	1	220	4	4
Guaiacol	1	2	200	10	35
Guaiacol	0.5	2	200	10	7
m-Cresol	1	2	220	6	31
m-Cresol	0.3	2	220	6	4
Cyclohexanol*	1	2	220	3	58
Cyclohexanol	0.5	2	220	3	36

TABLE 2

Substance vinylated (1 mole)	Vinylating agent (2 moles)	Reaction temperature	Duration of experiment (hours)	% Yield
Phenol	Propyne	220°	8	40
Phenol	Propadiene	220	8	20
Guaiacol	Propyne	200	10	35
Guaiacol	Propadiene	200	10	17

We know from the work of A. E. Favorskii [6] that the isomerization of acetylenic to allenic hydrocarbons is a reversible reaction. In the case of propadiene and propyne the equilibrium is shifted in the direction of propyne. Physicochemical calculations show [7] that the equilibrium mixture contains about 10% of propadiene and 90% of propyne at 200°. Propadiene readily isomerizes to propyne over various catalysts at elevated temperatures [8, 9]. In order to ascertain the behavior of propadiene under our conditions, we heated propadiene in an autoclave at 200° with 50% potassium hydroxide solution. It was found that propadiene isomerizes to propyne under these conditions, and the propyne was isolated as the acetylide. Propadiene did not polymerize [10] under these conditions. A comparison of the experiments on vinylation of phenols with propadiene and propyne (Tables 1 and 2) leads to the conclusion that propadiene is not the vinylating agent but isomerizes to propyne which then enters into the vinylation reaction [11].

The structure of the synthesized α-methyl-substituted ethers was confirmed by hydrolysis. α-Methylvinyl aryl ethers, like vinyl aryl ethers [9], are hydrolyzed under considerably more drastic conditions than α-methylvinyl alkyl ethers [12, 13].

EXPERIMENTAL

Propyne was prepared by the method of Hurd et al [5]. A weighed quantity of propyne was run into an autoclave which had previously been cooled with dry ice; propadiene [5, 14] was charged into an autoclave under similar conditions; the phenol had b. p. 181-182°, guiacaol b. p. 72° (6 mm), m-cresol b. p. 90° (12 mm), cyclohexanol b. p. 160.5°; the potassium hydroxide was the chem. pure grade.

1. Preparation of α-methylvinyl phenyl ether. Into a 1-liter Bergius rotating autoclave, fitted with electrical heater, thermocouple and acetylene manometer, were charged 135 g of phenol, 81 g of potassium hydroxide dissolved in 40 ml of water, and 115 g of propyne. The autoclave was heated for 4 hours at 220°. Maximum pressure 70 atm, residual pressure 20 atm. The autoclave was cooled, the propyne was collected in a trap immersed

* Cyclohexanol was vinylated without water.

in Dewar flask containing dry ice. 10 g of propyne was collected. The discharged product was a light-brown liquid which was distilled in vacuo. 1st fraction, b.p. 60-64° (12 mm), 82 g; 2nd fraction, 81-90° (12 mm), 5 g. The residue was 40 g of resin. The 1st fraction was dried with calcium chloride and distilled to give 80 g of α-methylvinyl phenyl ether (40%).

TABLE 3

Ether being hydrolyzed	Amount of ether determined (in %)
α-Methylvinyl phenyl	97.4, 96.0
α-Methylvinyl m-cresyl	97.2, 97.3
α-Methylvinyl guaiacyl	94.3, 92.7
α-Methylvinyl cyclohexyl	93.2, 94.0

B. p. 61-62° (16 mm), 168-169° (756 mm), d^{20}_4 0.9551, $n^{20}D$ 1.5050, MR_D 41.68; calculated 41.34.

Found %: C 80.53, 80.49; H 7.51, 7.58. $C_9H_{10}O$. Calculated %: C 80.60; H 7.52.

Literature data: b. p. 169°, d^{23}_4 0.998, $n^{22}D$ 1.5172 [1, 2].

2. Preparation of α-methylvinyl guiacyl ether. The reaction was performed in a 250-ml autoclave by the above procedure, starting from 62 g of guiacol, 28 g of potassium hydroxide dissolved in 14 ml of water, and 40 g of propyne. The autoclave was heated for 10 hours at 200°. Maximum pressure 84 atm, residual pressure 40 atm. 10 g of propyne was collected. The discharged product was fractionated with steam. The distillate was dried over calcium chloride and fractionally distilled in vacuo at 99-103° (18 mm). Elimination of guaiacol from the product was effected by dissolution in absolute ether and redistillation in vacuo. 26.3 g of α-methylvinyl guiacyl ether (32%) was obtained.

B. p. 71-72° (3 mm), 202-203° (742 mm), d^{20}_4 1.0392, $n^{20}D$ 1.5205, MR_D 47.98; calculated 47.60.

Found %: C 72.75, 72.72; H 7.22, 7.28. $C_{10}H_{12}O_2$. Calculated %: C 73.14; H 7.36.

3. Preparation of α-methylvinyl m-cresyl ether. 40 g of propyne, 54 g of m-cresol and 28.5 g of potassium hydroxide in 14 ml of water were charged into a 250-ml autoclave by the previous procedure. The mass was heated for 6 hours at 220°, and 117 g of a light-yellow, two-layered liquid was discharged. The upper layer was washed and dried and distilled to give 25 g of α-methylvinyl m-cresyl ether with b. p. 76.5-79° (14 mm). 38 g of resin remained in the flask. The viscous lower layer was steam-distilled to give 7 g of the ether. Both of the portions of ether were dried over calcium chloride. Total yield 27 g of α-methylvinyl m-cresyl ether (31%).

B. p. 78-79° (14 mm), d^{20}_4 0.9444, $n^{20}D$ 1.5051, MR_D 46.55; calculated 45.95.

Found %: C 81.04, 80.79; H 8.11, 8.14. $C_{10}H_{12}O$. Calculated %: C 81.16; H 8.14.

Literature data: b. p. 188-189°, d^{21}_4 0.978, $n^{21}D$ 1.5117 [2].

4. Preparation of α-methylvinyl cyclohexyl ether. 40 g of propyne, 50.7 g of cyclohexanol and 28.5 g of potassium hydroxide were charged into an autoclave by the above procedure. The autoclave was heated for 4 hours at 220°; 70 g of light-yellow liquid was discharged. It was distilled in vacuo. 1st fraction 52-53° (12 mm), 46 g; 2nd fraction 53-140° (12 mm), 7 g. Residue: 7 g of resin. Redistillation of the 1st fraction gave 44 g of α-methylvinyl cyclohexyl ether:

B. p. 52-53° (12 mm), 162-163° (752 mm), d^{20}_4 0.9176, $n^{20}D$ 1.4551, MR_D 41.48; calculated 42.74.

Found %: C 77.14, 76.94; H 11.61, 11.41. $C_9H_{16}O$. Calculated %: C 77.09; H 11.50.

5. Isomerization of propadiene to propyne in 50% potassium hydroxide solution. 21 g of propadiene, 7 g of potassium hydroxide in 7 ml of water were charged into a 250-ml autoclave. The mass was heated for 6 hours at 200°. Pressure 49 atm; 20 g of gas was discharged. Repeated passage through Ilosvay solution led to separation of a voluminous light-yellow precipitate of acetylide. The residue was 3 g of propadiene.

6. Hydrolysis of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers was effected with a solution of hydroxylamine hydrochloride at pH 2.9 [15]. Samples of ether weighing 0.2-0.3 g and 25 ml of hydroxylamine hydrochloride solution were charged into 40-ml ampoules which were then sealed, immersed in a boiling water bath and shaken for 4 hours at intervals of 15 minutes. The ampoules were then cooled and the contents transferred to a beaker. The acetone content was estimated from the amount of hydrochloric acid released. The

liquid was potentiometrically titrated with 0.1 N NaOH solution (methyl orange indicator) to pH 4. Results of the hydrolysis are presented in Table 3. The following formula was applied:

$$\% \text{ hydrolysis} = (a \cdot M \cdot 1.057 \cdot 100)/ w \cdot 10000$$

where a is the number of milliliters of 0.1 N sodium hydroxide solution consumed in titration of the acid released during the reaction (difference between the actual and a blank experiment); M is the molecular weight of the ether, 1.057 is a factor to allow for the reaction between acetone and hydroxylamine proceeding to the extent of 94.4% [16], and w is the weight of ether.

SUMMARY

1. A procedure was developed for the preparation of α-methylvinyl aryl and α-methylvinyl cyclohexyl ethers by the Favorskii-Shostakovskii method. α-Methylvinyl guaiacyl and α-methylvinyl cyclohexyl ethers were prepared for the first time.

2. It was shown that propadiene isomerizes in an alkaline medium to propyne, the latter being the vinylating agent.

3. The prepared ethers were hydrolyzed by a specially developed procedure.

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INTERACTION OF HALIDES OF TRIVALENT IRON WITH NICOTINE

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Reaction of nicotine with halides of zinc [1], mercury [2] and copper [3] in a medium of the corresponding hydrogen halides gave compounds whose composition and properties identify them as salts of nicotine and of free halogen acids with the general formula $HM\Gamma_3$ or $H_2M\Gamma_4$, where M is metal and Γ is chlorine, bromine or iodine.

In the present work we describe for the first time the results of a study of the reaction of nicotine with halides of trivalent iron both in presence of the corresponding hydrogen halides and in neutral, aqueous and alcoholic media.

EXPERIMENTAL

Nicotine was prepared and purified as previously described [4]. The ferric chloride was the chem. pure grade. Ferric bromide was prepared as described by Kariakin [5]; the iodide was prepared in similar fashion. Hydrochloric acid was purified by distillation; hydrobromic and hydriodic acids were prepared and purified as described in [5]. Ethyl alcohol (commercial) was twice distilled.

$FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$ was prepared by dissolving 2.75 g of ferric chloride in 20 ml of concentrated hydrochloric acid and adding 1.62 g of nicotine dropwise with vigorous stirring. The transparent brownish-yellow solution was put into a crystallizer and deposited yellow crystals after a few days at room temperature. Yield of uncrystallized product 67%. The substance was recrystallized from water and dried to constant weight at 100-105°. The salt had m. p. 188-189° (with decomp.); its solubility in water at 25° was 46.01%. It dissolved readily in methyl and ethyl alcohols; it was poorly soluble in acetone and insoluble in benzene and ether; the pH (determined potentiometrically) of this salt on dilution of 1 mole to 1000 liters was 2.74. The molecular electrical conductivity of the same solution at 25° was $1070\Omega^{-1}cm^2$. The halogen content was determined by the Volhard method, iron by the method given in [6]; nicotine was determined by titration with sulfuric acid in presence of methyl red after it had been distilled off from the alkali solution with steam.

Found %: Fe 14.09, 14.10; Cl 44.62, 44.73; $C_{10}H_{14}N_2$ 40.77, 40.69. $FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$. Calculated %: Fe 14.21; Cl 44.63; $C_{10}H_{14}N_2$ 40.79.

A compound of the same composition is obtained in a neutral aqueous or alcoholic medium. Its properties, however, are different. It is in the form of stout, transparent, brownish-yellow crystals, m. p. 156-157°; solubility in water at 18° 4.43%; the pH of this solution is 4.48. This solution turns cloudy at above 18°, and on boiling it deposits a brown solid. The pH of the solution on dilution of 1 mole to 1000 liters is 2.84. The molecular electrical conductivity of the same solution at 25° is $1030\Omega^{-1}cm^2$.

$FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$ was prepared by dissolving 2.95 g of ferric bromide in 20 ml of concentrated hydrobromic acid and adding 1.62 g of nicotine (dissolved in 3 ml of water) dropwise with stirring. The solution was placed in a crystallizer and deposited black crystals after a few days at room temperature. They were recrystallized from water. M. p. 182-183°.

Found %: Fe 8.95, 9.18; Br 64.23, 64.57; $C_{10}H_{14}N_2$ 26.49, 26.21. $FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$. Calculated %: Fe 9.01; Br 64.50; $C_{10}H_{14}N_2$ 26.15.

Solubility in water at 25° 50.62%. Good solubility in methyl and ethyl alcohols; insoluble in diethyl ether and benzene; poorly soluble in acetone. Molecular electrical conductivity after dilution of 1 mole to 1000

liters at 25°, 1037 $\Omega^{-1}cm_2$; pH 2.72.

$FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$ was prepared from 4.33 g of ferric iodide in 20 ml of concentrated hydriodic acid to which 1.62 g of nicotine was added. After a few days the solution deposited stout, black crystals. The salt is insoluble in water, benzene and diethyl ether; it is soluble in methyl and ethyl alcohols and acetone. Yield about 74%. M. p. 86-87°.

Found %: I 74.77, 73.98; $C_{10}H_{14}N_2$ 18.17, 19.04. $FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$. Calculated %: I 74.76; $C_{10}H_{14}N_2$ 18.97.

$FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$ was prepared from 4.33 g of ferric iodide dissolved in an equimolar quantity of hydriodic acid to which 1.62 g of nicotine was then added with stirring. Nearly black crystals came down after a few days and were washed with ether. Yield about 60%. Solubility in water at 25° 1.01%. Good solubility in methyl and ethyl alcohols; insoluble in benzene and ether. M. p. 98° (decomposes at 240°).

Found %: I 68.93, 68.17, 69.23; $C_{10}H_{14}N_2$ 21.72, 21.61. $FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$. Calculated %: I 69.86; $C_{10}H_{14}N_2$ 22.31; Fe 7.68.

It should be noted that the compound obtained from acid aqueous solution has a higher melting point (about 30° higher) and a much higher solubility than the compound obtained from water and alcohol. The crystals differ in color; the pH and molecular electrical conductivity of the aqueous solutions of these compounds are approximately identical. This phenomenon is evidently associated with the internal structure of these compounds and calls for closer investigation.

The melting point of solids obtained from acid solutions and which contain 2 moles of acid falls in passing from chlorides to iodides. The iodide with 1 mole of acid melts higher than that with 2 moles of acid. The halides are completely precipitated from the aqueous solutions of these salts by silver nitrate. The molecular electrical conductivity and pH of solutions of the chlorides and bromides indicate that free hydrogen, iron and halogen ions are present in solution. It therefore follows that the compounds prepared by us are salts of the corresponding chloro-, bromo- and iodoacids of iron which are completely dissociated into ions.

SUMMARY

1. The following complex salts of nicotine with ferric chloride, bromide and iodide and the corresponding hydrogen halides were prepared: $FeCl_3 \cdot C_{10}H_{14}N_2 \cdot 2HCl$; $FeBr_3 \cdot C_{10}H_{14}N_2 \cdot 2HBr$; $FeI_3 \cdot C_{10}H_{14}N_2 \cdot 2HI$; $FeI_3 \cdot C_{10}H_{14}N_2 \cdot HI$.

2. Compounds of nicotine with haloacids of iron of the type of $C_{10}H_{14}N_2 \cdot H_2MГ_5$ are completely dissociated into ions.

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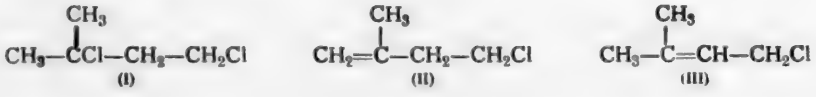
INVESTIGATIONS ON AMINES AND QUATERNARY AMMONIUM COMPOUNDS

X. PREPARATION OF ISOPRENE FROM α,β- AND γ,γ-DIMETHYLALLYL CHLORIDES

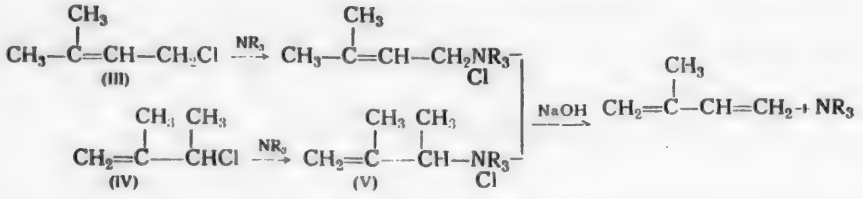
A. T. Babaian, G. M. Mkrian and R. S. Giuli-Kevkhian

Isoprene was first synthesized by Euler [1] by exhaustive methylation of β-methylpyrrolidine. Application of the Hofmann thermal cleavage of quaternary ammonium compounds is encountered in the patent literature on isoprene synthesis [2]. Ostromyslenskii claims [3] that dichloroisopentane (I), as well as the chloroisoamylenes (II and III) lose two molecules of hydrogen chloride to give isoprene when heated with amines possessing relatively low basicity, such as p-chloroaniline and quinoline.



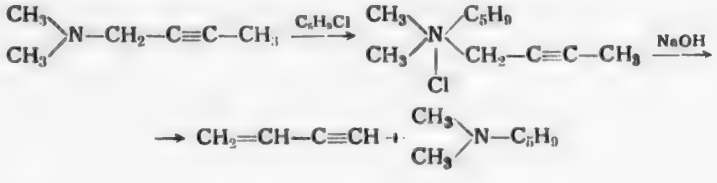
The above literature data and the results of investigations of dehydrochlorination and cleavage of quaternary ammonium salts with aqueous alkali, published in the preceding communications [4], indicated the possibility of development of a convenient method of preparation of isoprene from dichloroisopentanes and monochloroisoamylenes.

The present communication concerns the preparation of isoprene by alkaline cleavage of quaternary ammonium salts obtained by reaction of α,β- and γ,γ-dimethylallyl chlorides with tertiary amines.



Tertiary amines used in the work were dimethylisoamyl-, dimethyl(γ,γ-dimethylallyl)-, dimethylbenzyl- and dimethyl-(butyn-2-yl)-amines.

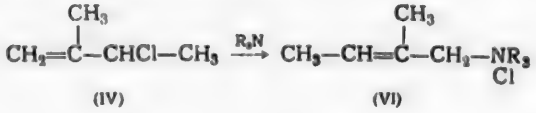
Reaction of (III) with amines goes energetically with heat development, and in some cases cooling is necessary. The chloride (IV) reacts slowly and prolonged heating is usually needed. Alkaline cleavage of the prepared quaternary ammonium salts led, except in the case of salts containing the butyn-2-yl radical, to formation of isoprene in yields of 58-85% and of the corresponding tertiary amine in yields of 67-89%. Alkaline cleavage of the quaternary ammonium salts obtained by interaction of the above-mentioned chlorides with 1-dimethylaminobutyne-2 led to formation of vinylacetylene and the corresponding tertiary amine.



These results testify to the lability of the butyn-2-yl radical and are consistent with our earlier results [4a, 5] on the cleavage of quaternary ammonium salts containing the butyn-2-yl radical.

Dimethyl-γ,γ-dimethylallylamine is also formed by alkaline cleavage of the quaternary ammonium salt obtained by interaction of γ,γ-dimethylallyl chloride with an aqueous solution of dimethylamine.

On the basis of the literature [6] we should expect chloride (IV) to react with tertiary amines to give not compound (V), which would be expected in a normal reaction, but its isomer (VI) or a mixture of both. The structure of the salts obtained has not yet been elucidated.



(IV) (VI)

Results of cleavage of the prepared quaternary ammonium salts by aqueous caustic alkali are presented in the table.

Isoprene was identified by its physical constants and by the preparation of the dihydrochloride [3]; the tertiary amines were identified by the melting points of the picrates.

EXPERIMENTAL

Quaternary ammonium salts were prepared by mixing equimolar quantities of alkyl halide and tertiary amine. The following procedure was used for cleavage of the ammonium salts: double the molar quantity of 40% aqueous sodium hydroxide was added gradually with stirring to the ammonium salt which was heated to 60-70° on a water bath. Heating was continued on a boiling water bath, during which operation the low-boiling products of cleavage (isoprene or vinylacetylene) were removed from the reaction mixture as soon as formed and collected in a receiver cooled with ice and salt. After distillation of the low-boiling product had ceased, the mixture was heated on a sandbath until the temperature of the evolved vapor had quickly risen to 70-75°; the objective of this measure was to extract the low-boiling products as completely as possible. The receiver was then changed, and the second component of the reaction (the amine) was distilled off from the reaction mixture. The amine layer was separated from the aqueous layer, dried and fractionally distilled.

1. Preparation of dimethyl-(α,β- or β,γ-dimethylallyl)-amine. An aqueous solution of sodium hydroxide was added to 9.95 g of dimethylbutynyl-(α,β- or β,γ-dimethylallyl) ammonium chloride heated to 65°. Vinylacetylene already started to come off at 68-70°. The cleavage reaction gave 8.4 g of vinylacetylene which distilled completely at 5.5-6° and gave a yellow precipitate with the Ilosvay reagent. The reaction mixture yielded 33.4 g (59.1%) of dimethyl-(α, β- or β,γ-dimethylallyl)-amine.

B. p. 111.5-117.5° (680 mm), d^{20}_4 0.7731, $n^{20}D$ 1.4270, MR_D 37.528; calculated 37.999.

Found %: N 12.49. $C_7H_{15}N$. Calculated %: N 12.39.

Picrate, m. p. 87-88°.

Found %: N 16.42. $C_{13}H_{18}O_7N_4$. Calculated %: N 16.37.

Methiodide, m. p. 139-140° [26].

2. Preparation of dimethyl-(γ,γ-dimethylallyl)-amine. A. An aqueous solution of sodium hydroxide was added to 17.2 g of dimethylbutynyl-(γ,γ-dimethylallyl) ammonium chloride. Cleavage took place at 79-80° and gave 2.6 g of vinylacetylene and 7.5 g (78.1%) of dimethyl-(γ,γ-dimethylallyl) amine.

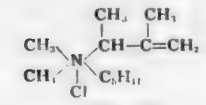
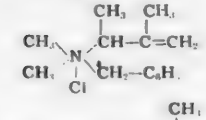
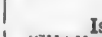
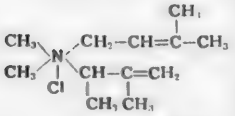
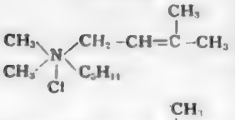
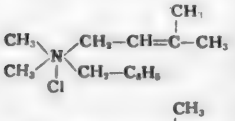
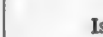
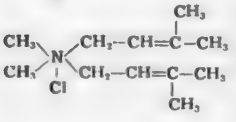
B. p. 116-118° (680 mm), d^{20}_4 0.7711, $n^{20}D$ 1.4276, MR_D 37.789; calculated 37.999.

Found %: N 12.21. $C_7H_{15}N$. Calculated %: N 12.39.

Picrate, m. p. 99-100°.

Found %: N 16.39. $C_{13}H_{18}O_7N_4$. Calculated %: N 16.37.

Methiodide, m. p. 160-161°.

Quaternary salt	M. p.	Ionic Cl (in %)		Products of cleavage by aqueous alkali	Yield (in %)	M. p. of amine picrate
		found	calc.			
	—	16.37	16.17	Isoprene 	65 72	— 130°
	170—171°	14.64	14.82	Isoprene 	59 88	— 96.5
	—	15.91	16.32	Isoprene 	62 75	— 87—88
	90—92	15.90	16.17	Isoprene 	58 67	— 130
	159—160	14.67	14.82	Isoprene 	85 89	— 96.5
	110—111	16.27	16.32	Isoprene 	67 85	— 99—100

B. 52.5 g of γ,γ-dimethylallyl chloride was stirred into 75 ml of 33% aqueous solution of dimethylamine. Heat was developed during the reaction. After the second layer had disappeared, a further 52 g of γ,γ-dimethylallyl chloride and 100 g of 40% aqueous sodium hydroxide was added. The aqueous layer was then subjected to cleavage by addition of 160 g of 50% sodium hydroxide solution. Cleavage took place at a temperature of 83-93° and gave 20 g of isoprene, which distilled completely at 29-32° (680 mm) (d^{20}_4 0.6817, $n^{20}D$ 1.4216) and 35 g of amine with b.p. 112-118° (600 mm); picrate with m. p. 99-100°. There was no depression of melting point of the mixture with the picrate of dimethyl-(γ,γ-dimethylallyl)-amine obtained by cleavage of dimethyl-(butyn-2-yl)-(γ,γ-dimethylallyl) ammonium chloride.

SUMMARY

1. It was shown that quaternary ammonium salts obtained by interaction of α,β- and γ,γ-dimethylallyl chlorides with dimethylisoamyl-, dimethylbenzyl- and dimethyl-(γ,γ-dimethylallyl) amines are cleaved by hot aqueous alkali with formation of isoprene and the corresponding tertiary amine.

2. Cleavage of quaternary ammonium salts containing the butyn-2-yl radical in addition to the α,β- or γ,γ-dimethylallyl radical leads to formation of vinylacetylene. 1,4-Cleavage of the butyn-2-yl radical accordingly goes with greater facility than cleavage of the other radicals.

3. It was established that alkaline cleavage of dimethyl-(γ,γ-dimethylallyl)-(α,β- or β,γ-dimethylallyl) ammonium chloride leads to formation of isoprene at the expense of the γ,γ-dimethylallyl radical.

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SUBSTITUTED HYDRAZIDES OF HYDROXYCARBOXYLIC ACIDS

II. SYNTHESIS OF ARYLHYDRAZIDES OF DIALKYLGLYCOLIC ACIDS

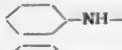
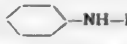
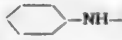
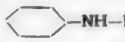
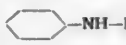
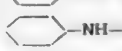
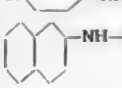
I. S. Berdinskii

The reaction of ethyl esters of β-arylhydrazides of oxalic acid with alkyl magnesium halides was studied in the course of development of the method described in the preceding communication [1]. Substances used were

$$Ar{-}NH{-}NH{-}CO{-}COOC_2H_5,$$

where Ar = C_6H_5; p-BrC_6H_4 and β-$C_{10}H_7$; in the components RMgX, R = C_2H_5, C_3H_7, iso-C_3H_7, C_4H_9, iso-C_5H_{11} and C_8H_{17}.

An experiment showed that reaction goes smoothly, and the arylhydrazides of dialkylglycolic acids are obtained in good yields. The structural formulas and melting points of the compounds that we obtained are given in the table. The synthesized arylhydrazides are colorless, crystalline substances, insoluble in water, soluble in common organic solvents; the arylhydrazides of acids with branched radicals are distinguished by higher melting points.

Compound no.	Formula	Melting point
(II)		121—122.5°
(III)		122.5—123.5
(IV)		164—166
(V)		127—128.5
(VI)		173—174
(VII)		101—102
(VIII)		135—136
(IX)		152—154

EXPERIMENTAL

Phenylhydrazide of diethylglycolic acid (II). 6.2 g of the ethyl ester of the β-phenylhydrazide of oxalic acid (I) was added to a solution of ethyl magnesium bromide prepared from 19.7 g of ethyl bromide and 4.4 g of magnesium. Finally, the reaction mass was heated on a water bath for 30 minutes and decomposed with dilute hydrochloric acid. The reaction product was extracted with ether. Yield 6.3 g (95.4%). Insoluble in water, soluble in ether, benzene, alcohol, toluene. Needles (from toluene), m. p. 121-122.5°.

Found %: N 12.83, 12.71. $C_{12}H_{18}O_2N_2$. Calculated %: N 12.61.

Phenylhydrazide of dipropylglycolic acid (III). Starting substances: 6.2 g of (I), 4.4 g of magnesium and 22.1 g of propyl bromide. Yield 7.1 g (95.3%). Sparingly soluble in ether and gasoline; more easily soluble in alcohol and toluene. Needles (from gasoline), m. p. 122.5-123.5°.

Found %: C 67.17, 67.02; H 8.77, 8.78; N 10.98, 10.91. $C_{14}H_{22}O_2N_2$. Calculated %: C 67.20; H 8.80; N 11.20.

Phenylhydrazide of diisopropylglycolic acid (IV). Starting substances: 2.1 g of (I), 1.4 g of magnesium and 4.7 g of isopropyl chloride. Yield 2.3 g (92%). Insoluble in gasoline, sparingly soluble in ether and dioxane; soluble in alcohol, toluene, glacial acetic acid, chloroform and carbon tetrachloride. Needles (from carbon tetrachloride), m. p. 164-166°.

Found %: N 10.91, 11.48. $C_{14}H_{22}O_2N_2$. Calculated %: N 11.20.

Phenylhydrazide of dibutylglycolic acid (V). Reactants were 6.2 g of (I), 24.7 g of butyl bromide and 4.4 g of magnesium. Yield 7.3 g (87.9%). Soluble in alcohol, benzene, gasoline and toluene. Prisms (from toluene), m. p. 127-128.5°.

Found %: N 9.82, 9.85. $C_{16}H_{26}O_2N_2$. Calculated %: N 10.07.

Phenylhydrazide of diisoamylglycolic acid (VI). Reaction was effected with 6.2 g of (I), 27.2 g of isoamyl bromide and 4.4 g of magnesium. Yield 8.3 g (91.21%). Sparingly soluble in ether, more readily soluble in toluene, alcohol and gasoline. Needles (from toluene), m. p. 173-174°.

Found %: N 8.80, 8.84. $C_{18}H_{30}O_2N_2$. Calculated %: N 9.15.

Phenylhydrazide of dioctylglycolic acid (VII). Starting substances: 5.5 g of (I), 31 g of n-octyl bromide and 3.9 g of magnesium. Yield 9 g (87.4%). Soluble in alcohol, ether, toluene and chloroform. Needles (from alcohol), m. p. 101-102°.

Found %: N 6.88, 7.29. $C_{24}H_{42}O_2N_2$. Calculated %: N 7.18.

p-Bromophenylhydrazide of dibutylglycolic acid (VIII). Reaction was effected with 2.9 g of the ethyl ester of the p-bromophenylhydrazide of oxalic acid, 8.4 g of butyl bromide and 1.5 g of magnesium. Yield 3.4 g (97.14%). Readily soluble in ether, more difficultly soluble in alcohol, toluene, and glacial acetic acid. Needles arranged in clusters (from toluene), m. p. 135-136°.

Found %: N 7.71, 7.62. $C_{16}H_{25}O_2N_2Br$. Calculated %: N 7.84.

β-Naphthylhydrazide of dibutylglycolic acid (IX). Starting substances: 2.0 g of the ethyl ester of the β-naphthylhydrazide of oxalic acid, 6.2 g of butyl bromide and 1.1 g of magnesium. Yield 2.3 g (92.0%). Insoluble in ether, soluble in toluene, alcohol and glacial acetic acid. Needles collected in clusters (from glacial acetic acid), m. p. 152-154°.

Found %: N 8.24, 8.39. $C_{20}H_{28}O_2N_2$. Calculated %: N 8.53.

SUMMARY

The reaction between alkyl magnesium halides and esters of β-arylhydrazides of oxalic acid can be recommended for the preparation of arylhydrazides of dialkylglycolic acids. A series of previously undescribed representatives of this class of substances were prepared and their properties were studied.

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Perm Institute of Pharmacy

* Original Russian pagination. See C. B. Translation.

SYNTHESIS OF SOME BIFUNCTIONAL COMPOUNDS CONTAINING SULFIDIC SULFUR

V. I. Lutkova and B. B. Berezina

Dinitriles, diamines and dicarboxylic acids containing sulfidic sulfur may be of interest as intermediates for production of polyamides, polyurethanes and polyethers. It is well-known that the synthesis of certain compounds of this group can be effected via δ-chlorovaleronitrile [1]. Information about these syntheses is inadequate. Syntheses and properties of the products are not described, but only preparative schemes are presented. The objective of the present investigation was to develop methods of synthesis of δ-chlorovaleronitrile, di-(4-nitrilotetramethylene) sulfide, di-(4-carboxytetramethylene) sulfide and di-(5-aminopentamethylene) sulfide.

EXPERIMENTAL

δ-Chlorovaleronitrile. A mixture of 65 g of KCN, 254 g of 1,4-dichlorobutane and 200 g of adiponitrile was stirred at 135-140° for 10-12 hours. After cooling, the precipitate was filtered off, dissolved in water, and extracted from the water with benzene. The benzene solution was dried with calcined sodium sulfate and the benzene was distilled off. The residue was combined with the filtrate and fractionated in vacuo to give a 62% yield of product, calculated on the 1,4-dichlorobutane consumed.

B. p. 115-117° at 28 mm, d^{20}_{20} 1.0536, $n^{20}D$ 1.4430.

Found %: N 11.0. C_5H_8NCl. Calculated %: N 11.9.*

Di-(4-nitrilotetramethylene) sulfide. A mixture of 30 g of sodium sulfide nonahydrate, 45 g of δ-chlorovaleronitrile, 100 g of diethyleneglycol and 10 ml of water was heated to the boil (120°) and stirred at this temperature for 6 hours. After cooling, the precipitated NaCl was filtered off. The upper layer of liquid was collected from the filtrate, and the residue of reaction product was extracted from the lower layer with chloroform. After the chloroform had been driven off, the residue was combined with the separated upper layer of liquid, which contained di-(4-nitrilotetramethylene) sulfide, and distilled at 192-194° (3.5 mm). Yield 68% reckoned on the δ-chlorovaleronitrile consumed. The product was a yellowish liquid which gave the characteristic reaction for sulfur with sodium nitroprusside; $n^{20}D$ 1.4863; d^{20}_{20} 1.0230.

Found %: C 61.14; H 7.7; N 14.2. $C_{10}H_8N_2S$. Calculated %: C 61.2; H 8.1; N 14.2.

Di-(4-carboxytetramethylene) sulfide. A mixture of 24.5 g of di-(4-nitrilotetramethylene) sulfide and 100 ml of conc. HCl was heated on a boiling water bath for 4 hours and then poured into a porcelain beaker containing cold water; the acid came down in the form of crystals with m. p. 94-95°, acid number 478.3, calculated acid number 478.6. Yield 67%. A number of esters were prepared from the acid.

Di-(5-aminopentamethylene) sulfide. A solution of 20 g of di-(4-nitrilotetramethylene) sulfide in 200 ml of anhydrous ethanol was heated to the boil, and 40 g of sodium in small pieces was added at such a rate that the resulting foam did not disappear; the solution was then heated for 2 hours until the sodium had completely disappeared. After the mass had cooled, 200 ml of water was added to decompose the alcoholate; the alcohol was distilled off and the residual mixture separated into layers. The top layer was distilled under nitrogen in 2 ml portions at 146-148°. Yield 71.3%. The prepared di-(5-aminopentamethylene) sulfide is a colorless liquid; $n^{20}D$ 1.5000; d^{20}_{20} 1.0401.

* According to [2], b. p. 115-118° at 28 mm; $n^{20}D$ 1.4447; yield 48%.

Found %: C 59.5; H 12.6; N 13.55; NH_2 (Van Slyke method) 15.0. $C_{10}H_{24}N_2S$. Calculated %: C 58.8; H 11.7; N 13.7; NH_2 15.6.

SUMMARY

Methods were developed for the preparation of δ-chlorovaleronitrile, di-(4-nitrilotetramethylene) sulfide, di-(4-carboxytetramethylene) sulfide and di-(5-aminopentamethylene) sulfide.

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TRANSFORMATION REACTIONS OF METHYLOLMETHACRYLAMIDE

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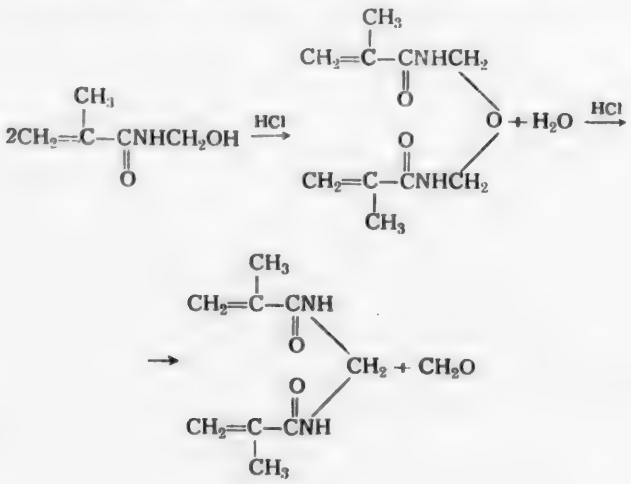
V. N. Efremova and I. K. Ulezlo

Feuer and Lynch were the first to synthesize unsaturated methylolamides by reacting acrylamide and methacrylamide with paraformaldehyde in either dichloroethane or carbon tetrachloride medium in the presence of a catalyst (colloidal sodium). When heated in organic solvents with hydrochloric acid the methylolmethacrylamide and methylolacrylamide were converted by them to methylene(bis)acrylamides [1]. According to existing literature data, certain methylolacyl- and arylamides served as model compounds in elucidating the complex mechanism of the reactions that take place in the condensation of urea with formaldehyde. Based on the data of Einhorn [2] and of Zigeuner [3], methylolamides in alkaline medium form diamidomethyl ethers, whereas the corresponding methylene compounds are formed under the influence of acids. Zigeuner and co-workers also expressed the theory that it is possible for diamidomethyl ethers to be formed in weakly acid medium [4].

In one of our experiments on the synthesis of methylolmethacrylamide by the method of Feuer and Lynch we isolated, together with the desired methylolmethacrylamide, a substance with m. p. 80.5-81.5°, which proved to be the previously unknown dimethacrylamidodimethyl ether. Repeated attempts made subsequently to again isolate this compound from the products of the indicated reaction for the synthesis of methylolmethacrylamide proved unsuccessful, which caused us to make a more detailed study of the transformation reactions of methylolmethacrylamide.

Attempts to synthesize dimethacrylamidodimethyl ether by reacting methylolmethacrylamide with benzoyl chloride in alkaline medium, similar to the procedure used by Zigeuner [5], proved unsuccessful. On the assumption that dimethacrylamidodimethyl ether should be formed as an intermediate product in the synthesis of methylenedimethacrylamide, we studied the behavior of methylolmethacrylamide in the presence of acid catalysts. When methylolmethacrylamide was heated with a small amount of hydrochloric acid it was converted to dimethacrylamidodimethyl ether. When the catalyst concentration was increased the dimethacrylamidodimethyl ether was converted to the previously known methylenedimethacrylamide



According to the data of Feuer and Lynch, methylolmethacrylamide when heated in the presence of mineral acids and boron trifluoride is polymerized to infusible and insoluble polymers, which is evidence of their tridimensional structure. Our experiments on the matter revealed that methylolmethacrylamide is also polymerized under the influence of peroxide initiators, and here, depending on the polymerization conditions, it is possible to obtain either linear or tridimensional polymers. When exposed to ultraviolet radiation methylolmethacrylamide is polymerized to an infusible solid. Bulk polymerization in the presence of benzoyl peroxide yields a glassy polymer, insoluble in water and the common organic solvents. Polymerization in aqueous medium permits obtaining a linear polymer that is soluble in water, glycol and glycerin.

EXPERIMENTAL

Methacrylamide (I) was obtained by a modification of the Arcus method [6]. Instead of the tedious operation of isolating (I) from dilute aqueous ammonia solution by steam-distillation under reduced pressure, we cooled the homogeneous reaction mixture to −40°. The obtained crystals of (I) were filtered and dried at 50-60°. The yield of (I) (m. p. 108-110°) was 67-70%. The obtained (I) can we used without further purification for the synthesis of methylolmethacrylamide.

Preparation of catalysts. Sodium metal was converted to thin sheets under xylene. Sodium ethylate was used as a finely divided powder.

Methylolmethacrylamide (II). a) Synthesis by the method of Feuer and Lynch [1]. The results of the experiments made to study the influence of the amount of catalyst on the reaction rate are summarized in the table. In all of the experiments the amount of (I) taken was 71 g (in 1 liter of carbon tetrachloride), and the bath temperature was 45-50°.

Influence of the Amount of Catalyst on the Formation Rate of Methylolmethacrylamide

Catalyst	Amount (in %)	Reaction time (in minutes)
Sodium metal	0.1	60
	0.2	45
	0.3	30
	0.4	18
Sodium ethylate	0.5	30
	1.0	3-5
	1.5	0.5-1

From the data given in the table it can be seen that the formation rate increases with increase in the amount of catalyst.

b) The reaction was run in toluene with 1.5% of catalyst (sodium ethylate). On conclusion of reaction, which took 15 minutes, we isolated (II) in 64% yield from the reaction mixture.

Dimethacrylamidodimethyl ether (III). A mixture of 40 g of (II) and 200 ml of dichloroethane, the latter containing 0.14 g of hydrochloric acid, was heated with stirring for 70 minutes at 45-50°. After removal of the solvent and two recrystallizations from benzene we obtained crystals with m. p. 80.5-81.5°. Yield of (III) 16 g (43.4%).

Found %: C 56.50; H 7.6; N 13.18. M 212.6. $C_{10}H_{16}O_3N_2$. Calculated %: C 56.56; H 7.6; N 13.2. M 212.14.

The tetrabromide was analyzed for bromine.

Found %: Br 60.08. $C_{10}H_{16}O_3N_2Br_4$. Calculated %: Br 60.09.

Methylenedimethacrylamide (IV). A mixture of 4 g of (III) and 20 ml of dichloroethane, the latter containing 1.4 g/liter of hydrochloric acid, was heated at 60° for 5 hours. On conclusion of reaction a precipitate of 0.6 g of crystals deposited from the reaction mixture. Removal of the solvent yielded 2.8 g of (IV) with m. p. 161-164°. Yield 81.6%. Methylenedimethacrylamide melts at 162-163° [1].

Polymerization of (II). a) Under the influence of ultraviolet light. We used a PRK-2 lamp as the light source. The wavelength region in the vicinity of $\lambda \sim 3000$ A was used for the polymerization. 1.5 g of (II) with m. p. 53.5-54.5° (% N 12.18) was placed on a watch glass at a distance of 50 cm from the light source. Irradiation at 35° was maintained for 19 hours. At the end of reaction the polymer was purified by extraction with ethyl acetate. After drying we obtained 1.204 g (80.3%) of a polymer, insoluble in water and organic solvents (% N 12.14).

b) In solvent. Ten grams of (II) was dissolved in 100 ml of water, containing 0.075 mole/liter of hydrogen peroxide. The mixture was heated with stirring at 60-70° in a stream of carbon dioxide for 7 hours. At the end of heating a viscous solution of the polymer was obtained. The polymer was isolated from solution by precipitation in methyl alcohol. The precipitate was filtered and dried to give 5.3 g (53%) of a cottony polymer. The polymer is soluble in water, glycol and glycerin, and shows slight swelling in pyridine. Its characteristic viscosity, determined in an Ostwald viscosimeter, is 0.41.

SUMMARY

1. The behavior of methylolmethacrylamide under the influence of acid catalysts was studied. We were the first to synthesize and characterize dimethacrylamidodimethyl ether, which was converted to methylenedimethacrylamide when the concentration of the catalyst was increased.

2. The polymerization of methylolmethacrylamide in aqueous solution using an initiator (hydrogen peroxide) gave a linear polymer.

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OXIDATION OF α,β-UNSATURATED METHYL KETONES WITH SODIUM HYPOBROMITE

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The oxidation of α,β-unsaturated methyl ketones with hypohalites is a method that is used for the preparation of certain α,β-unsaturated acids. Unsaturated ketones of the alkyl aryl series are converted to the corresponding unsaturated acids in yields up to 88% [1, 2]. The data existing in the literature on the oxidation of α,β-unsaturated ketones of the aliphatic series relate to ketones with a branched chain of carbon atoms; the yields of unsaturated acids in this case range from 23 to 49% [3-6].

When the indicated reaction was applied to α,β-unsaturated methyl ketones with a straight carbon chain, and specifically to 3-nonen-2-one and 3-decen-2-one, we obtained the corresponding α,β-unsaturated acids, also in a yield of about 40%. Together with this, we also established that α,β-dihydroxy acids are formed here (α,β-dihydroxycaprylic acid in 10% yield and α,β-dihydroxypelargonic acid in 20% yield, respectively). Variation in the reaction conditions, such as changing the caustic concentration (from 0.2 to 2%), the amount of active bromine (from 3 to 8%), and also the temperature (from 10 to 70°), exerts very little influence on the formation of the dihydroxy acids.

The formation of the corresponding α,β-dihydroxy acids was also observed when other α,β-unsaturated ketones with a straight carbon chain were oxidized. Thus the oxidation of 3-undecen-2-one and 3-tridecen-2-one gave respectively α,β-dihydroxydecanoic acid in 10% yield and α,β-dihydroxydodecanoic acid in 20% yield. The yield of the α,β-unsaturated acids was about 30%.

In view of the fact that the formation of dihydroxy acids was not observed in the above mentioned studies on the oxidation with hypohalites of α,β-unsaturated methyl ketones of the aliphatic series with a branched chain, we repeated some of these experiments. We were unable to establish the presence of dihydroxy acids in the reaction mixture when either mesityl oxide or 5-methyl-3-hexen-2-one was oxidized with sodium hypobromite. This makes it possible to assume that the presence of branching near the double bond in the molecule of the starting ketone makes the formation of dihydroxy acids in the discussed reaction difficult.

The formation of α,β-dihydroxy acids when α,β-unsaturated ketones are oxidized with hypobromite is probably due to the hydration of the initially obtained glycidic acids. For example, it is indicated that a glycidic acid is formed when cinnamaldehyde is oxidized with sodium hypobromite [7]. Other evidence in support of this is the fact that all of the α,β-dihydroxy acids obtained by us proved to have different melting points from the α,β-dihydroxy acids formed in the oxidation of the corresponding α,β-unsaturated acids with permanganate, but identical with the melting points of the dihydroxy acids obtained from the glycidic acids. Thus, the α,β-dihydroxy acid isolated by us from the oxidation of 3-decen-2-one with sodium hypobromite had the same melting point (116°) as the dihydroxy acid obtained in the oxidation of α,β-nonenoic acid with performic acid [8]. This same acid was obtained by us when we subjected the ethyl ester of hexylglycidic acid, synthesized by the Darzens method [9], to hydration and then hydrolysis.

The oxidation of α,β-unsaturated methyl ketones can be depicted by the scheme shown on page 1329.

TABLE 1

Properties of Unsaturated Ketones

Name of ketone	Yield (in %)	B. p. (pressure in mm)	n_D^{25}	d_4^{20}	MR_D found	MR_D calc.	Amt. of ketone (in %)•	Bromine no. found••	Bromine no. calc.	M. p. of derivatives: semicarbazone	M. p. of derivatives: 2,4-dinitrophenylhydrazone	N content in derivatives (in %) found	N content in derivatives (in %) calc.	Remarks
Benzalacetone•••	63.7	128–133° (10)	—	—	—	—	99.3	108	109	—	—	—	—	—
Mesityl oxide	—	129–133	1.4480	—	—	—	—	171	163	—	—	—	—	Commercial product used
5-Methyl-3-hexen-2-one	54.2	65–68 (13)	1.4380	0.8545	34.34	34.07	100	150	142	125.5°	—	24.65, 24.50	24.84	—
3-Nonen-2-one	70	72 (6)	1.4470	0.8478	44.09	43.30	100	120	113	116–117	—	21.25, 21.36	21.32	New
3-Decen-2-one	74	82–85 (5)	1.4480	0.8474	48.64	47.92	99.2	111	103	117–118	—	19.51, 19.65	19.90	—
3-Undecen-2-one	59	98–99 (5)	1.4485	0.8631	52.15	52.54	92	87	95	—	73°	16.35, 16.41	16.09	New
3-Tridecen-2-one	65	106 (6)	1.4522	0.8513	62.16	61.77	105	86	81	—	75	15.09, 14.81	14.89	New

• Determined by the oximation method of L. N. Petrova and E. N. Novikova [12].

•• Determined by the Kaufmann method.

••• Obtained by the condensation of benzaldehyde with acetone in the presence of 10% aqueous NaOh solution [13].

TABLE 2

Properties of Unsaturated Acids

Starting ketone	Name of unsaturated acids	Yield (in %)	Boiling point (pressure in mm)	$n^{20}D$	d^{20}_4	MR_D		Acid Number		Bromine number (Kaufmann method)	
						Found	Calc.	Found	Calc.	Found	Calc.
Mesityl oxide	Dimethylacrylic	44	M. p. 68.5-69.5°	—	—	—	—	559.2	560	161.3	160
5-Methyl-3-hexen-2-one	Isohexenoic	72	98 (6)	1.4490	0.9527	32.06	30.97	489	491	130	140
3-Nonen-2-one	Δ^2-Octenoic	42.5	130-131 (6)	1.4588	0.9442	41.00	40.21	392	394	108	112
3-Decen-2-one	Δ^2-Nonenoic	36.8	134-136 (4)	1.4600	0.9385	45.32	44.83	355	359	94	102
3-Undecen-2-one	Δ^2-Decenoic	33	147-148 (8)	1.4610*	0.9365*	49.75	49.44	328	329	87.8	94
3-Tridecen-2-one	Δ^2-Dodecenoic	21	141-142 (3)	1.4615	0.9265	58.70	58.68	292	282	80.1	80.8

* The determinations were made at 23°

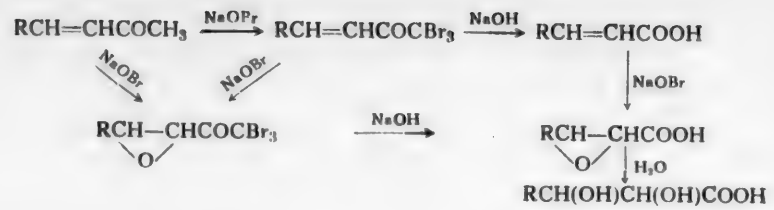
TABLE 3

Properties of α,β-Dihydroxy Acids, Obtained in the Oxidation of Unsaturated Methyl Ketones with Hypobromite

Name of acids	Melting point	Literature melting point for dihydroxy acids obtained from corresponding unsaturated acids		Acid number		Amount of hydroxyl (in %)		Elemental analysis (in %)						Yields of dihydroxy acids (in %)
		By oxidation with potassium permanganate	By oxidation with per-acids	Found	Calc.	Found*	Calc.	of dihydroxy acid				of silver salt		
								Found		Calc.		Found	Calc.	
								C	H	C	H	Ag	Ag	
α,β-Dihydroxyoctanoic	114-115°	118-119° [14]	—	318	314	28	28.63	53.84, 53.90	9.12, 9.08	53.93	8.98	38.18	38.00	10.0
α,β-Dihydroxypelargonic	116-117°**	123 [15]	118° [8]	300	295	27.1	26.84	56.65, 56.25	9.52, 9.42	56.84	9.47	36.26	36.20	20.0
α,β-Dihydroxydecanoic	108-110	121-123 [16]	—	278.6	274	16.24	25.0	58.35, 58.35	9.72, 9.78	58.88	9.80	—	—	10.4
α,β-Dihydroxydodecanoic	108-109	123 [17]	—	245	241	18.6	21.9	61.27, 61.26	10.00, 10.17	62.00	10.34	—	—	20.0

* Determined by the Zerevitinov method. The poor agreement of the results in the last two cases is apparently due to the poor solubility of the dihydroxy acids in xylene and diisobutyl ether.

** The mixed melting point with the dihydroxy acid obtained from the hydration and hydrolysis of the hexylglycidic acid ester was not depressed. The mixed melting point with the acid obtained from the oxidation of the nonenoic acid with potassium permanganate was 97-99°.



EXPERIMENTAL

The unsaturated ketones were obtained by the V. I. Esafov method [10], i.e., by the condensation of the corresponding aldehydes with acetone in the presence of piperidine and glacial acid. The properties of the unsaturated ketones are listed in Table 1.

Oxidation of unsaturated ketones with sodium hypobromite. Sodium hypobromite* (containing 5-7% active bromine and 1-1.5% sodium hydroxide), taken in 20% excess, was added with vigorous stirring to the unsaturated ketone at 35-40°. Then the reaction mixture was kept at 28-35° for 3-4 hours; the excess hypobromite was destroyed with bisulfite solution, and the alkaline solution was first extracted with diethyl ether and then acidified with concentrated hydrochloric acid until acid to Congo. The product obtained on acidification was separated and steam-distilled, in which connection the unsaturated acid came over in the distillate, while the α,β-dihydroxy acid remained in the distillation flask. The unsaturated acids were isolated from the distillate in conventional manner and then vacuum-distilled; the α,β-dihydroxy acids were extracted with ether, and after removal of the solvent, were purified by washing with either cyclohexane or petroleum ether. The properties of the obtained α,β-unsaturated acids and α,β-dihydroxy acids are given in Tables 2 and 3.

Preparation of α,β-dihydroxypelargonic acid by the Darzens method. The condensation of enanthole with ethylmonochloroacetate was run in conventional manner. The yield of ethyl hexylglycidate was 18.6%.

B. p. 122-123° (7 mm), $n^{20}D$ 1.4450, d^{20}_4 0.9828.

Literature [9]: b. p. 117-119° (6 mm); $n^{20}D$ 1.4448, d^{20}_4 0.9882.

The glycidic acid ester (19 g) was refluxed for 3 hours with 60 g of 10% NaOH solution. The alkaline solution was first extracted with ether and then acidified. The acid that separated here was extracted with ether; the ether extract was worked up in conventional manner. After removal of the solvent we obtained 7 g of crystalline α,β-dihydroxypelargonic acid with m. p. 101-105°. Yield 38.8%. After washing with cyclohexane the acid had m. p. 115-116°, acid number 295 (calcd. 294), and content of hydroxyl groups 26.1% (calcd. 26.8%). Its mixed melting point with the α,β-dihydroxypelargonic acid obtained by us from the oxidation of 3-decen-2-one with sodium hypobromite was not depressed.

SUMMARY

It was shown that the oxidation of aliphatic α,β-unsaturated methyl ketones of normal structure with sodium hypobromite yields, together with α,β-unsaturated acids, the corresponding α,β-dihydroxy acids. The formation of dihydroxy acids was not observed when methyl ketones, having a branched chain near the ethylenic bond, were oxidized.

It was established that the obtained dihydroxy acids are different from the α,β-dihydroxy acids formed in the oxidation of unsaturated acids with potassium permanganate, but are identical with the dihydroxy acids obtained in the hydration of the corresponding glycidic acids.

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SYNTHESIS OF SOME ESTERS OF 4,4'-DIHYDROXYDIPHENYL SULFONE AND CARBOXYLIC ACIDS

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A number of sulfone derivatives have proved to be highly active toward acid-resistant microorganisms, especially those responsible for tuberculosis and leprosy. Thus, at the present time 4,4'-diaminodiphenyl sulfone is the preferred agent used in the treatment of leprosy in French Guiana.

Much less attention has been devoted to the hydroxy derivatives of diphenyl sulfone, although these could be expected to show bactericidal action. According to [1], 4,4'-diamono-2,2'-dihydroxydiphenyl sulfone shows in vitro antibactericidal activity toward M. tuberculosis, streptococci, B. pyogenes, B. coli and staphylococci. Diacetyldihydroxydiphenyl sulfone can be used in the treatment of bacterial infections (miningococci and gonococci) [2].

Our objective was to synthesize some neutral esters of 4,4'-dihydroxydiphenyl sulfone with various carboxylic acids of the aliphatic, aromatic and heterocyclic series. Statements exist in the literature that esters of 4,4'-dihydroxydiphenyl sulfone are obtained by the condensation of the latter with acids in the presence of phosphorus oxychloride [3]. We utilized the same method. The compounds needed for the syntheses were either purchased or synthesized by us using the methods described in the literature, and were checked for purity by determining the chemical constants, and in some cases also by analysis. To synthesize the esters we took dry dihydroxydiphenyl sulfone and ground it intimately in a mortar with the proper acid (1 part of sulfone and 2 parts of acid), after which the mixture was transferred to a flask and heated in a glycerin bath at 120-140°; then the calculated amount of phosphorus oxychloride was cautiously added in drops. After all of the phosphorus oxychloride had been added the melt was heated until hydrogen chloride ceased to evolve. Then the melt was cooled and treated with 5% soda solution; this resulted in the removal of both organic and inorganic acids, and also of unreacted dihydroxydiphenyl sulfone. The ester that remained was purified by recrystallization.

The ester of α-bromoisovaleric acid and dihydroxydiphenyl sulfone was obtained by heating α-bromoisovaleryl bromide with the sodium salt of dihydroxydiphenyl sulfone.

The obtained esters are either white or light-yellow powders, difficultly soluble in water, and soluble in alcohol, acetone and dioxane. The ester of the sulfone and nicotinic acid is readily soluble in dilute hydrochloric acid. The esters suffer hydrolysis when heated with 10% aqueous caustic solution. They are hydrolyzed in the cold with alcoholic caustic.

The properties of the 14 esters obtained by us are given in the Table.

EXPERIMENTAL

4,4'-Dihydroxydiphenyl sulfone. One gram-mole of p-hydroxybenzenesulfonic acid was placed in a flask and then 13 ml of 98% sulfuric acid and 1 g-mole of phenol were added. The temperature was raised rapidly to 165° and the mixture kept at this temperature for 6 hours. Then the temperature was raised to 195-200° and heated for another 6 hours. The mixture was cooled and the precipitate was recrystallized three times from hot water. M. p. 238-239° (literature [4]: m. p. 240-241°). Yield 80-85%.

Diacetyl-p-aminosalicylic acid. Five grams of the sodium salt of p-aminosalicyclic acid was dissolved at the boil in a mixture of 250 ml of benzene and 20 ml of acetic anhydride. The mixture was refluxed for 4

Esters of 4,4'-Dihydroxydiphenyl Sulfone and Carboxylic Acids $RCOOC_6H_4SO_2C_6H_4OOCR$

R	Empirical formula of ester	Recrystallization solvent*	Yield (in %)	External appearance**	Melting point	S content (in %) found	S content (in %) calc.
n-C_4H_9	$C_{22}H_{26}O_6S$	al	50—55	wc	88—89°	7.95	7.68
α-C_4H_8Br	$C_{22}H_{24}O_6SBr_2$	d	32—35	wc	73—74	5.22	5.55
o-$CH_3COOC_6H_4$	$C_{30}H_{22}O_{10}S$	al	87—90	wp	288—290	5.23	5.57
p-$CH_3COOC_6H_4$	$C_{30}H_{22}O_{10}S$	al	85—90	wp	300	5.17	5.57
$C_6H_5CH=CH$	$C_{30}H_{22}O_6S$	d	85—90	wp	270—273	6.43	6.27
m-$O_2NC_6H_4CH=CH$	$C_{30}H_{20}O_{10}N_2S$	d	85—90	wp	202—205	5.65	5.33
$C_6H_5CHBrCHBr$	$C_{30}H_{22}O_6Br_4S$	al	85—90	wp	170—172	4.34	3.86
$C_6H_5CH_2CH_2$	$C_{30}H_{30}O_6S$	al	85—90	wp	180—182	5.89	6.20
$C_6H_5CONHCH_2$	$C_{30}H_{24}O_8N_2S$	ac	80—85	wp	238—240	5.66	5.59
o-$CH_3CONHC_6H_4$	$C_{30}H_{24}O_8N_2S$	d	50—55	y	208—210	5.22 (N)	4.88 (N)
m-$CH_3CONHC_6H_4$	$C_{30}H_{24}O_8N_2S$	d	50—55	y	195—197	4.63 (N)	4.88 (N)
p-$CH_3CONHC_6H_4$	$C_{30}H_{24}O_8N_2S$	d	50—55	y	216—219	5.11 (N)	4.88 (N)
C_5H_4N	$C_{24}H_{16}O_6N_2S$	ac	85—90	y	203—204	7.05	6.95
4(CH_3CONH), 2(CH_3COO), C_6H_3	$C_{34}H_{28}O_{12}N_2S$	d	51—55	y	155—158	3.96 (N)	4.06 (N)

* al — alcohol, d — dioxane, ac — acetone.

** wp — white powder, wc — white crystals, y — yellow powder.

hours. Crystals of diacetyl-p-aminosalicyclic acid deposited on cooling. M. p. 286-288° (from a mixture of benzene and dioxane in a 5:1 ratio).

Found %: N 6.25, 6.11. $C_{11}H_{11}O_5N$. Calculated %: N 5.90.

The acetyl derivatives of the o-, m- and p-aminobenzoic acids were obtained in a similar manner.

Ester of dihydroxydiphenyl sulfone and α-bromoisovaleric acid. A mixture of 1.47 g of the sodium salt of dihydroxydiphenyl sulfone and 2.45 g of α-bromoisovaleryl bromide was heated in a glycerin bath at 110-130° for 2 hours. The melt after cooling was treated with 1% soda solution, and then with hot water. The crude ester was recrystallized from a small volume of dioxane. Yield 0.8 g. M. p. 73-74°.

Ester of dihydroxydiphenyl sulfone and cinnamic acid. A mixture of 2.5 g of dihydroxydiphenyl sulfone and 2.96 g of cinnamic acid was intimately ground in a mortar and then heated in a flask in a glycerin bath at 120-140°; then the phosphorus oxychloride (0.8 ml) was added in drops. Heating was continued until hydrogen chloride ceased to evolve (3-3.5 hours). The melt after cooling was treated with 5% soda solution; this made it possible to remove both inorganic and organic acids, and also unreacted dihydroxydiphenyl sulfone. The ester was purified by recrystallization from dioxane. White crystalline powder; m. p. 271-272°.

The other esters of acids and dihydroxydiphenyl sulfone were obtained in a similar manner. The obtained esters proved to be inactive toward staphylococci (both white and golden), dysentery bacillus, diphtheria bacillus and capsule microbes. The ester of diacetyl-p-aminosalicyclic acid and dihydroxydiphenyl sulfone shows slight in vitro activity against tubercle bacillus.*

SUMMARY

We synthesized and characterized the neutral esters of 4,4'-dihydroxydiphenyl sulfone and the acids: valeric, α-bromoisovaleric, p- and o-acetoxybenzoic, o-, m- and p-acetamidobenzoic, cinnamic, m-nitrocinnamic, phenylpropionic, dibromophenylpropionic, hippuric, nicotinic and diacetyl-p-aminosalicyclic.

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CYCLOALKYLATION OF AROMATIC COMPOUNDS

XIV. CONDENSATION OF CYCLOHEXANOL WITH SOME AROMATIC HYDROCARBONS

N. G. Sidorova and I. A. Poliker

Continuing our investigations on the alkylation of aromatic compounds with cyclic alcohols [1], we studied the condensation of the xylenes, mesitylene, naphthalene and fluorene with cyclohexanol in the presence of aluminum chloride.

The cyclohexylation of the xylenes has received little study. The first paper on this subject describes the condensation of m-xylene with cyclohexyl bromide in the presence of ferric chloride [2]. Later Bodroux [3], who studied the alkylation of aromatic compounds with cyclohexene in the presence of aluminum chloride, obtained the cyclohexyl derivatives of a large number of hydrocarbons, including those of m- and p-xylene. Recently the cyclohexyl ester of p-toluenesulfonic acid has been used to cyclohexylate m- and p-xylene [4].

The only method used to introduce the cyclohexyl group into mesitylene was by condensing the latter with cyclohexene in the presence of aluminum chloride [3].

Various methods have been used to cyclohexylate naphthalene. Bodroux [5] condensed naphthalene with cyclohexene and obtained 19% of mixed cyclohexylnaphthalenes, containing predominantly the β-isomer, and 2,6-dicyclohexylnaphthalene. A similar reaction is described in an American patent [6]. Pokrovskaia and Stepantsova [7] employed the Bodroux method and, depending on the ratios of the reactants, obtained products with a variable amount of mono- and polycyclohexylnaphthalenes (up to the tetra-substituted derivative). Later Buu-Hoi and Cagniant [8] employed the same method to obtain 2,6-dicyclohexylnaphthalene. The condensations of naphthalene with cyclohexene and cyclohexanol in the presence of boron fluoride are also described [9, 10]. The best yield (63%) of β-cyclohexylnaphthalene was obtained with cyclohexanol. Of interest is the fact that the disubstituted product obtained in the presence of boron fluoride has the structure of 1,4-dicyclohexylnaphthalene, whereas the 2,6-isomer is formed with aluminum chloride [11].

Of special interest is the condensation of cyclohexanol with fluorene, since the nuclear alkylation of fluorene has hardly been studied. Only three papers on this subject are known – the condensation of fluorene with benzyl chloride in the presence of zinc [12], the alkylation of fluorene with propylene in the presence of phosphoric acid [13], and the reaction of fluorene with some olefins and alkyl chlorides [14].

To avoid side reactions we ran the alkylation of the xylenes, mesitylene and naphthalene with cyclohexanol using the minimum amount of aluminum chloride, a large excess of the hydrocarbon, and a low temperature.

In the case of mesitylene the best results were obtained with 0.7 g-equiv. of aluminum chloride (based on cyclohexanol), and in the remaining cases with 0.82-0.84 g-equiv.

We obtained 4-cyclohexyl-1,2-dimethylbenzene in 71.5% yield from o-xylene. The reaction was somewhat poorer with p-xylene; under similar conditions the yield of 2-cyclohexyl-1,4-dimethylbenzene was 68.6%. The alkylation of m-xylene went with extreme ease, and an 86% yield of 5-cyclohexyl-1,3-dimethylbenzene was obtained from it. The structure of this product was shown by its oxidation to trimesic acid, which was then converted to the trimethyl ester. Previous investigators [2, 3] also obtained the same hydrocarbon from m-xylene. However, in a recent paper [15] the structure of 4-cyclohexyl-1,3-dimethylbenzene is assigned to the condensation product of m-xylene with cyclohexene in the presence of aluminum chloride.

The condensation of mesitylene with cyclohexanol gave a 35.9% yield of 2-cyclohexyl-1,3,5-trimethylbenzene. However, this yield is not lower than that obtained in the condensation of mesitylene with cyclohexene [3].

The alkylation of naphthalene gave about a 59% yield of a monocyclohexylnaphthalene fraction, composed mainly of the β-isomer, and about a 40% yield of a dicyclohexylnaphthalene fraction, in which the presence of the 2,6-isomer was shown.

A comparison of the obtained results with literature data, in addition, shows that cyclohexanol is the most convenient alkylating agent for the introduction of the cyclohexyl radical into aromatic compounds. The yields obtained with it are frequently higher than those obtained with either cyclohexene or cyclohexyl chloride, and the reaction products do not contain polymeric impurities, which is the case when cyclohexene is used.

The condensations of fluorene with cyclohexanol proceed with considerable difficulty. An excess of the hydrocarbon being alkylated leads to a reduction in the yield in this case. For this reason the reactions were run either with equimolar amounts of fluorene and cyclohexanol or with an excess of the latter. The aluminum chloride was taken in an amount of 0.85 g-equiv. based on the cyclohexanol. The maximum yield of crude cyclohexylfluorene obtained by us under these conditions was 37%, calculated on the weight of fluorene taken for reaction. However, a part of the fluorene remains unchanged here and can be recycled.

Although the use of excess cyclohexanol leads to an increased yield of cyclohexylfluorene, still the product obtained in such case is less pure than when equimolar amounts of the reactants are taken.

EXPERIMENTAL

The condensations were run in conventional apparatus, without a stirrer. The aluminum chloride was slowly added in small portions to the mixture of hydrocarbon and cyclohexanol; the mixture was shaken periodically. In the case of naphthalene and fluorene the reactions were run in a solution of dearomatized petroleum ether. (The aromatics were removed from the petroleum ether by chromatographic adsorption on silica gel.) After all of the aluminum chloride had been added the mixture was allowed to stand overnight, and then it was heated on the water bath. The mixture after cooling was decomposed with dilute hydrochloric acid, and the hydrocarbon layer was dried over calcium chloride and distilled from sodium. The liquid reaction products were redistilled from sodium. The results of the different condensations are summarized in the Table.

Conditions and Results of the Condensations

Aromatic hydrocarbon	Mole ratio $ArH:C_6H_{11}OH:AlCl_3$	Heating regime		Yield of products (in %)	
		temp.	time (in hrs)	mono-substituted	disubstituted
o-Xylene	8.3 : 1 : 0.66	65—75°	4	55.8	—
	8.3 : 1 : 0.82	65—75	4	71.5	—
	8.3 : 1 : 0.98	65—75	4	71.5	—
m-Xylene	8.2 : 1 : 0.84	65—75	4	85.9	—
p-Xylene	8.1 : 1 : 0.80	65—75	2	59.8	—
	8.1 : 1 : 0.84	65—75	4	68.6	—
Mesitylene	3.6 : 1 : 0.86	60—80	4	27.2	—
	5 : 1 : 0.71	60—80	4	35.9	—
Naphthalene	3.2 : 1 : 0.69	45—75	4	53.3	34.2
	3.2 : 1 : 0.84	45—75	4	58.8	39.7
Fluorene	1 : 1 : 0.85	65—100	6	—	—
	1 : 1 : 0.85	65—100	18	32.9	—
	1.5 : 1 : 0.85	65—100	50	24.2	—
	0.5 : 1 : 0.85	65—100	17	37.0	—

The following products were isolated.

4-Cyclohexyl-o-xylene

B. p. 140-142° (17 mm), $n^{20}D$ 1.5271, d^{20}_4 0.9386, MR_D 61.69; calculated 61.05.

Found %: C 88.80; H 10.74. $C_{14}H_{20}$. Calculated %: C 89.29; H 10.71.

Oxidation with dilute (1:4) nitric acid (by long boiling with 15-20 volumes of acid) gave trimellitic acid with m. p. 218° (from water).

5-Cyclohexyl-m-xylene

B. p. 138-139° (15 mm), $n^{20}D$ 1.5225, d^{20}_4 0.9343, MR_D 61.52; calculated 61.05. Literature: b. p. 266-268°, $n^{18}D$ 1.5250, d^{18}_4 0.931 [3].

Oxidation with nitric acid gave trimesic acid with m. p. above 300°. Treatment of the acid with diazomethane gave the trimethyl ester with m. p. 140-143° (from alcohol).

2-Cyclohexyl-p-xylene

B. p. 138-140° (18 mm), $n^{20}D$ 1.5230, d^{20}_4 0.9348, MR_D 61.53; calculated 61.05. Literature: b. p. 261-262°, $n^{18}D$ 1.529, d^{18}_4 0.9360 [3].

Oxidation gave trimellitic acid with m. p. 218°.

Cyclohexylmesitylene

B. p. 146-148° (12 mm), $n^{20}D$ 1.5275, d^{20}_4 0.9337, MR_D 66.68; calculated 65.67. Literature: b. p. 283-284.5°, $n^{9}D$ 1.535, d^{9}_4 0.946 [3].

Oxidation with dilute nitric acid gave an acid with m. p. 215-230°.

β-Cyclohexylnaphthalene

B. p. 162-164° (6 mm), 145-148° (2 mm), $n^{20}D$ 1.5985, d^{20}_4 1.0211, MR_D 70.31; calculated 67.17.

β-Cyclohexylnaphthalene on cooling congealed to a white crystalline mass. The crystals, pressed on porous plate, had m. p. 31°. Literature: b. p. 190-195° (15 mm), 170-180° (3 mm); m. p. 31° [7, 9].

Dehydrogenation of β-cyclohexylnaphthalene with selenium at 300-350° gave β-phenylnaphthalene with m.p. 100° (from alcohol). According to the literature, β-phenylnaphthalene melts at 102° [16].

Dicyclohexylnaphthalene. B. p. 210-220° (5 mm); the main portion distilled at 220°. On long standing the fraction crystallized. The crystals, pressed on porous plate and recrystallized from acetone, melted at 150-151°, which corresponds to 2,6-dicyclohexylnaphthalene [10, 11].

Cyclohexylfluorene. The compound was isolated as the fraction with b. p. 180-190° (5 mm), which immediately crystallized. After several recrystallizations from alcohol the compound was obtained as tiny white crystals with m. p. 133°. Readily soluble in benzene, ether and hot alcohol.

Found %: C 92.24; H 8.56. $C_{19}H_{20}$. Calculated %: C 91.88; H 8.12.

The mixing of benzene solutions of picric acid and cyclohexylfluorene gave a dark-red color, but the picrate underwent decomposition when its isolation was attempted.

SUMMARY

The condensation of cyclohexanol with the xylenes, mesitylene, naphthalene and fluorene in the presence of aluminum chloride gave the cyclohexyl derivatives of these hydrocarbons.

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SYNTHESIS OF 1,4-DIISOPROPYLBENZENE AND SOME OF ITS TRANSFORMATIONS

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Dialkylbenzenes are usually formed in the synthesis of monoalkylbenzenes and are regarded as undesirable by-products. It was shown recently that it is possible to convert dialkylbenzenes to phthalic acids and diatomic phenols. Of especial interest here was the synthesis of terephthalic acid and hydroquinone by the oxidation of 1,4-dialkylbenzenes. In connection with this we undertook a broad investigation on the alkylation of monoalkylbenzenes with olefins.

The alkylation of toluene and ethylbenzene with pseudobutylene in the presence of $BF_3 \cdot H_3PO_4$ was described in one of our communications [1], and it was shown that the catalyst $BF_3 \cdot H_3PO_4$ directs the secondary butyl radical mainly in the para-position and makes it possible to obtain 1-methyl-4-sec-butylbenzene and 1-ethyl-4-sec-butylbenzene in yields of 81-84 and 71-73%, respectively.

In this paper we studied the alkylation of isopropylbenzene with propylene in the presence of $BF_3 \cdot H_3PO_4$. It was found that 1,4-diisopropylbenzene is obtained in 73% yield if the isopropylbenzene, propylene and catalyst are taken in the mole ratio 4:1:0.26 and the reaction is run at 98-100°. Under the same conditions, but with the mole ratio of reactants and catalyst taken equal to 3:1:0.2, the yield of 1,4-diisopropylbenzene is 61%, and if run at a temperature of 52-55° the yield drops to 19%.

We studied the liquid-phase oxidation of 1,4-diisopropylbenzene with atmospheric oxygen in the presence of various initiators to the mono- and dihydroperoxides.

As our studies revealed, the oxidation of 1,4-diisopropylbenzene proceeds in such manner that for some time the hydroperoxide accumulates up to a certain maximum, after which the hydroperoxide begins to decompose, and its amount in solution decreases. At 110° such a maximum is reached in 12-14 hours, and at 85° it is reached in 20-40 hours, in both cases depending on the initiator.

The mixed initiator, manganese resinate and cobalt acetate, with calcium hydroxide as the additive, is a more vigorous oxidation initiator at 110° than either the manganese resinate or cobalt acetate taken separately, with the same additive.

The addition of sodium stearate to the mixed initiator of manganese resinate, cobalt acetate and calcium hydroxide accelerates the oxidation and permits obtaining a 51% yield of the hydroperoxide in 17 hours, whereas when the indicated mixture of initiators is used without the addition of sodium stearate the extent of oxidation reaches only 33% at 110° in 16 hours, after which the hydroperoxide begins to decompose. The addition, besides sodium stearate, of small amounts of sodium hydroxide permits oxidizing 1,4-diisopropylbenzene to the hydroperoxide to the extent of 59% in 22 hours.

Calcium hydroxide also accelerates the oxidation and stabilizes the hydroperoxide, thus making it possible to obtain more profound oxidation. Thus, when 1,4-diisopropylbenzene is oxidized in the presence of manganese resinate, cobalt acetate and sodium stearate the extent of oxidation is 33% in 39 hours at 85°. Under the same conditions, but with the addition of calcium hydroxide to the indicated mixture of initiators, the oxidation proceeds to the extent of a 54% yield of hydroperoxide in 24 hours.

The oxidation proceeds mainly toward forming the diisopropylbenzene monohydroperoxide, which when cleaved in acid medium gives 4-isopropylphenol in about 90% yield. A small amount of diisopropylbenzene dihydroperoxide is also formed, which cleaves to hydroquinone.

Cleavage of 1,4-Diisopropylbenzene Hydroperoxide

Taken for cleavage						Amount of cleavage products obtained (in %)			
Solution of hydroperoxide in diisopropylbenzene (in g)	Hydroperoxide content (in %)	Calculated as 100% hydroperoxide (in g)	Sulfuric acid (in g)	Acetone (in g)	Cleavage temperature	Acetone	4-Isopropylphenol	Hydroquinone	Recovered 1,4-diisopropylbenzene
122.7	30.7	37.7	200 (20%)	—	91°	47.9	32.6	—	53.4
55.2	56.6	31.2	200 (10%)	—	96-98	65.6	26.1	—	22.1
43.2	39.0	16.8	200 (7%)	—	99-100	66.9	41.0	—	25.9
73.6	33.3	24.5	50 (7%)	—	98-99	74.6	67.4	—	48.1
216.5	17.2	37.2	0.5 (conc.)	5	65	82.1	87.6	—	167.1
62.5	83.1	53.9	150 (conc.)	85	58	86.0	84.8	13.2	7.4
154.8	59.0	91.3	2.8 (conc.)	2 ml	100	84.6	65.6	14.6	62.1

EXPERIMENTAL

Synthesis of 1,4-diisopropylbenzene. Expt. 1. Into a round-bottomed flask, fitted with stirrer, thermometer and gas-inlet tube, was charged 414 g of $BF_3 \cdot H_3PO_4$ and 3 kg of technical isopropylbenzene with b. p. 149-154°, d^{20}_4 0.8620 and $n^{20}D$ 1.4912. The mixture was heated to 98-100° and then 403 g of propylene (mole ratio of reactants and catalyst 4:1:0.26) was added at this temperature with vigorous stirring in 3 hours. Then the reaction products were allowed to stand at room temperature for 12 hours, after which the upper hydrocarbon layer was separated from the lower catalyst layer and heated for 1 hour at 100° with calcium hydroxide (7% on weight of alkylate). After such treatment the alkylate was separated from the calcium hydroxide and fractionally distilled through a column with an efficiency of 15-18 theoretical plates.

About 50 g of low-boiling products (d^{20}_4 0.7112, $n^{20}D$ 1.4005) and 2071 g of unreacted isopropylbenzene distilled at atmospheric pressure. The residue was vacuum-distilled. Here we obtained 1130 g (73%) of 1,4-diisopropylbenzene. A residue of 120 g (8%) of polyisopropylbenzenes remained in the distillation flask.

Expt. 2. The reaction of 3 kg of isopropylbenzene, 525 g of propylene and 414 g of $BF_3 \cdot H_3PO_4$ (mole ratio 3:1:0.2) for 3 hours at 98-103° gave 1238 g (61%) of 1,4-diisopropylbenzene and 138 g (7%) of polyisopropylbenzenes. Here 1973 g of unreacted isopropylbenzene was recovered.

Expt. 3. The reaction of 3 kg of isopropylbenzene, 617 g of propylene and 414 g of $BF_3 \cdot H_3PO_4$ (mole ratio 2.75:1:0.17) for 4 hours at 52-55° gave 444 g (19%) of 1,4-diisopropylbenzene and 26 g (1%) of polyisopropylbenzenes. Here 2640 g of unreacted isopropylbenzene was recovered.

1,4-Diisopropylbenzene (distilled twice) is a mobile liquid with a pleasant odor.

B. p. 209-211°, d^{20}_4 0.8570, $n^{20}D$ 1.4898. Literature [2]: b. p. 210.4°, d^{20}_4 0.8568, $n^{20}D$ 1.4898.

2,5-Diisopropylacetanilide. Ten grams of 1,4-diisopropylbenzene was added to a nitrating mixture [10 g of HNO_3 (d 1.42) and 15 g of H_2SO_4 (d 1.84)] with ice-salt cooling at such a rate that the reaction temperature did not exceed 30°. Then the reaction mixture was heated for 1 hour at 50°, and the nitration products after cooling were separated from the acid layer, neutralized with soda solution, washed with water, dried, and distilled. We obtained 7.3 g (57%) of 2-nitro-1,4-diisopropylbenzene as a light-yellow oily liquid with a bird cherry odor. B. p. 128-130° (1.5-2 mm), d^{20}_4 1.0168, $n^{20}D$ 1.5220.

A mixture of 6.02 g of 2-nitro-1,4-diisopropylbenzene, 15 ml of ethyl alcohol and 0.3 ml of concentrated hydrochloric

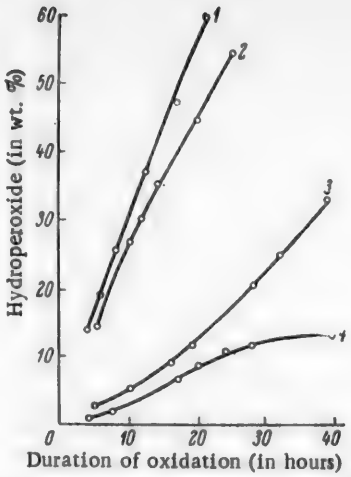

Fig. 1. Oxidation rate of 1,4-diisopropylbenzene at 85°. 1) manganese resinate + calcium hydroxide + sodium stearate + sodium hydroxide; 2) manganese resinate + cobalt acetate + calcium hydroxide + sodium stearate; 3) manganese resinate + cobalt acetate + sodium stearate; 4) sodium stearate.

Fig. 2. Oxidation rate of 1,4-diisopropylbenzene at 110°. 1) manganese resinate + cobalt acetate + calcium hydroxide; 2) cobalt acetate + calcium hydroxide; 3) manganese resinate + zinc oxide; 4) manganese resinate + calcium hydroxide; 5) cobalt acetate.

acid was heated to the boil, and after adding 51** g of iron filings in 4 portions, was boiled for 4 hours. Then 0.5 g of solid sodium hydroxide was added, and the 2-amino-1,4-diisopropylbenzene (5.3 g of crude product) was steam-distilled. The amine without purification was mixed with 25 g of 10% acetic acid, and then 3 g of acetic anhydride and one drop of concentrated sulfuric acid were added to the mixture with stirring. The acetanilide, obtained as a white flocculent precipitate, after short standing was filtered and then recrystallized from petroleum ether. It had m. p. 80-80.5°, which corresponds to 2,5-diisopropylacetanilide [3].

Liquid-phase oxidation of 1,4-diisopropylbenzene with atmospheric oxygen. Air was passed at a rate of 12-18 liters/hour through a porous glass plate sealed in the bottom of the vessel into a mixture of 162 g (1 mole) of 1,4-diisopropylbenzene and definite amounts of initiators* at a given temperature. (The reaction mixture gradually assumed a dark-yellow color.)

The amount of hydroperoxide in percent was determined iodometrically at intervals of 2 to 4 hours. The solution of diisopropylbenzene hydroperoxide is a dark-yellow viscous liquid with a sharp ozone odor. 94% of the hydroperoxide has b. p. 120-126° at 1 mm, d^{20}_4 0.9932, $n^{20}D$ 1.5128. According to the literature [4] diisopropylbenzene monohydroperoxide has $n^{20}D$ 1.5120.

The results of the oxidations run at 85° are plotted in Fig. 1, and those obtained at 110° are plotted in Fig. 2. The maximum concentration of diisopropylbenzene hydroperoxide, obtained in the presence of various initiators, was 59.8%.

The cleavage of 1,4-diisopropylbenzene hydroperoxide to phenol and acetone, using either sulfuric acid or a mixture of sulfuric acid and acetone, was effected in the following manner. A solution of diisopropylbenzene hydroperoxide was placed in a three-necked flask, fitted with stirrer, reflux condenser and thermometer, and then the sulfuric acid was added slowly with vigorous stirring. The degree of cleavage was determined iodometrically. The cleavage products were treated with ammonia, the acetone was evaporated, and the residue was vacuum-distilled. Here the diisopropylbenzene distilled first, and then the 4-isopropylphenol and hydroquinone.

When dilute sulfuric acid was used for the cleavage it was necessary to heat the mixture to 90-100° to start the reaction, and this favored intense tarring of the cleavage products.

The use of large amounts of sulfuric acid also favors tar formation. The reaction proceeds calmly when small amounts of concentrated sulfuric acid and acetone are used for the cleavage, the mixture heats up to 60-100° in a matter of 10-40 minutes, and only small amounts of tarry products

* Manganese resinate 0.5-5 mg, other initiators 100-500 mg.

** As in original – Publisher's note.

are formed. Some of the data on the cleavage of the hydroperoxide under different conditions are given in the Table.

4-Isopropylphenol was obtained as white needles with m. p. 59-60° (from petroleum ether), d^{20}_4 0.9898, $n^{20}D$ 1.5228. Literature [5]: m. p. 61°, d^{20}_4 0.990, $n^{20}D$ 1.5228.

4-Isopropylphenoxyacetic acid. A mixture of 1 g of 4-isopropylphenol, 5 ml of 33% sodium hydroxide and 1.5 g of chloroacetic acid was heated for 1 hour on the boiling water bath. The solution was cooled, diluted with 10 ml of water, acidified with hydrochloric acid, and extracted with 50 ml of ether. The ether solution was washed with water, shaken with 25 ml of 5% soda solution, and again acidified with dilute hydrochloric acid. The tiny white needles of 4-isopropylphenoxyacetic acid obtained after recrystallization from hot water had m.p. 80°, which agrees with the literature.

Methyl ether of 4-isopropylphenol. Into a 100-ml round-bottomed flask, connected through a two-way opening with a reflux condenser, was charged 50 ml of ethyl alcohol and 3.68 g of sodium metal. The sodium ethylate solution was cooled and mixed with 22.6 g of 4-isopropylphenol and 31.5 g of methyl iodide. Then the mixture was heated on the boiling water bath until neutral, and the flask was connected through the second opening to a descending condenser; after removal of the alcohol by distillation the residue was treated with a small amount of water to dissolve sodium iodide, and the 4-isopropylanisole was extracted with ether. The solution was shaken with dilute aqueous sodium hydroxide (to remove 4-isopropylphenol), dried over calcium chloride, and distilled. We obtained 19.98 g (80%) of the ether.

B. p. 95-96° at 19 mm, d^{17}_4 0.9495, $n^{17}D$ 1.5044. Literature [5]: d^{17}_4 0.9495, $n^{17}D$ 1.5045.

The cleavage of 32.6 g of 28% diisopropylbenzene hydroperoxide (9.13 g, calculated as 100% monohydroperoxide) by heating with 40 ml of 30% potassium hydroxide solution at 120° for 1 hour gave 5.87 g (70%) of dimethylcumenylcarbinol with b. p. 94-99° (mainly 97°) at 1.5-2 mm, d^{20}_4 0.9777, $n^{20}D$ 1.5100, MR_D 54.50; calculated 55.54.

Dimethylcumenylcarbinol on standing changes into white needle crystals with m. p. 58° (from petroleum ether).

Isolation of diisopropylbenzene dihydroperoxide and its cleavage to hydroquinone. A mixture of 19.7 g of 86% diisopropylbenzene hydroperoxide and 30 ml of an alcoholic solution of 5.4 g of sodium ethylate was stirred well with ice-salt cooling. The obtained precipitate was filtered, washed twice with ether, and dried in a vacuum-desiccator. Then it was placed in water and carbon dioxide was passed through the mixture. Here the sodium salt was converted to diisopropylbenzene dihydroperoxide, which deposited as fine colorless crystals (2.6 g). After recrystallization from a mixture of alcohol and petroleum ether the compound was obtained as grayish needles with m. p. 141°, which agrees with the literature [4].

A mixture of 1.86 g of diisopropylbenzene dihydroperoxide and 15 ml of 20% hydrochloric acid was placed in a 50-ml round-bottomed flask, fitted with a reflux condenser, and heated on the water bath to 67°. Here the dihydroperoxide suffered vigorous cleavage, and the mixture frothed and became homogeneous. After cooling to room temperature the cleavage products were treated with ether, the ether extract dried over sodium sulfate, and then separated from the latter by decantation. Removal of the ether gave 0.71 g (78.5%) of hydroquinone with m. p. 168.5° (after recrystallization from water).

SUMMARY

The alkylation of isopropylbenzene with propylene in the presence of $BF_3 \cdot H_3PO_4$ was studied and conditions were found under which 1,4-diisopropylbenzene is obtained in 73% yield.

Some initiators were found and also the conditions under which 1,4-diisopropylbenzene is oxidized with atmospheric oxygen to give a 59% yield of the hydroperoxide.

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ABSORPTION SPECTRUM OF 1,3-CYCLOHEXADIENE IN THE 220-300 mμ REGION

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The absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region has been investigated in a number of papers [1-3]; however the data of the various authors are not in complete agreement.

The positions of the maxima and the absorption coefficients, found by various authors, are given in Table 1.

TABLE 1

Positions of Absorption Maxima and Values of Molecular Absorption Coefficients for 1,3-Cyclohexadiene Based on the Data of Various Authors

Authors	Method used to prepare 1,3-cyclohexadiene	State of the compound when taking the absorption spectra	λ_{max} (in mμ)	log ε
Stark and Levy [1]	From 1,2-dibromocyclohexane	Vapor	213	–
			260	–
Allsopp [2]	–	Solution in cyclohexane	256	3.98
			267.5	3.82
Henri and Pickett [3]	From ethyl-Δ^2-cyclohexenyl ether	Vapor	251.2	3.87
			243.6	3.83
			241.4	3.86
			234.2	3.63
			232.1	3.62
		Solution in hexane	265.3	3.78
			256	3.90
			247.5	3.73

The data given in Table 1 indicate that the results obtained by the different authors in studying the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region differ among themselves primarily in the number of maxima appearing on the absorption curve. It is possible that the differences in the data of the various authors are due to insufficient purity of the investigated compound. In this connection we investigated the absorption spectrum in the ultraviolet region of a 1,3-cyclohexadiene specimen* that we felt justified in considering to be purer than the specimens available to the other investigators.

EXPERIMENTAL

Prior to experiment the 1,3-cyclohexadiene was distilled from $MgSO_4$. It had the following physical constants: b. p. 80.5°, d^{20}_4 0.8440, $n^{20}D$ 1.4746. The 1,3-cyclohexadiene specimen reacted with maleic anhydride without leaving a residue. The hexane and ethyl alcohol, used as solvents, were also redistilled before each

* Prepared in the Industrial Catalysis Laboratory of the Institute of Chemistry of the Academy of Sciences of White Russia SSR.

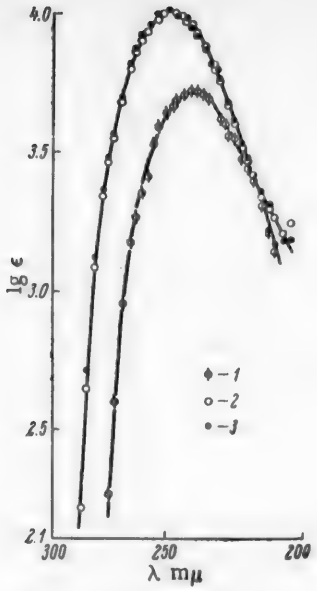

Fig. 1. Molecular absorption coefficient of 1,3-cyclohexadiene vapors (1) and of solutions of 1,3-cyclohexadiene in hexane (2) and in alcohol (3).

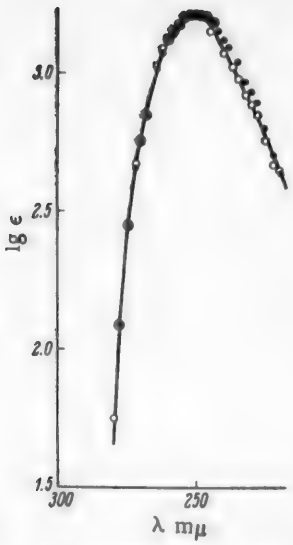

Fig. 2. Reproducibility of the data in measuring the molecular absorption coefficient of 1,3-cyclohexadiene vapors in different experiments.

TABLE 2

Molecular Absorption Coefficients of 1,3-Cyclohexadiene

Vapors		Solution in hexane		Solution in alcohol		Vapors		Solution in hexane		Solution in alcohol	
(in mμ)	lg ε	(in mμ)	lg ε	(in mμ)	lg ε	(in mμ)	lg ε	(in mμ)	lg ε	(in mμ)	lg ε
220	3.15	214	3.25	214	3.19	252	3.72	256	4.00	258	4.00
222	3.21	217	3.21	217	3.18	253	3.71	258	4.01	260	4.00
225	3.31	220	3.27	220	3.17	254	3.71	260	4.00	262	3.99
228	3.40	222	3.30	222	3.22	256	3.69	262	3.98	265	3.95
230	3.44	225	3.34	225	3.26	257	3.67	264	3.96	268	3.91
232	3.48	228	3.40	228	3.32	258	3.66	266	3.93	270	3.86
235	3.55	230	3.45	230	3.37	259	3.64	268	3.90	272	3.81
237	3.56	232	3.52	232	3.43	260	3.63	270	3.86	275	3.69
238	3.60	235	3.61	235	3.61	262	3.59	272	3.80	278	3.56
240	3.62	237	3.67	237	3.67	264	3.53	275	3.68	280	3.47
242	3.66	240	3.76	240	3.76	266	3.41	278	3.55	282	3.36
244	3.69	242	3.82	242	3.80	268	3.35	280	3.46	285	3.12
246	3.71	245	3.88	245	3.87	270	3.26	282	3.34	288	2.71
248	3.72	248	3.93	248	3.92	272	3.17	285	3.08	292	2.06
249	3.72	250	3.96	250	3.95	275	2.95	288	2.64	295	1.53
250	3.72	252	3.98	252	3.97	278	2.59	290	2.21	298	1.02
251	3.72	254	3.99	255	3.99	280	2.26	—	—	—	—

experiment. They practically failed to absorb light in the ultraviolet region clear up to 215 mμ. An SF-4 spectrophotometer was used to take the absorption spectra. The concentration of 1,3-cyclohexadiene and the thickness of the cuvette were chosen in such manner that the optical density was within the range 0.3-0.9, i.e., in the range where the spectrophotometric measurements are most accurate. To obtain small concentrations of 1,3-cyclohexadiene in the gas phase we introduced a drop of an alcohol solution of 1,3-cyclohexadiene of

known weight and concentration into the cuvette, which was then completely vaporized. The slit width selected was the minimum for making measurements at the given wavelengths. In general the slit width changed from 0.2 mm at λ 300 mμ to 1 mm at λ 220 mμ.

The absorption curves for 1,3-cyclohexadiene in the vapor state, and also in hexane and alcohol solutions, are shown in Fig. 1, while the numerical values of the absorption coefficients are given in Table 2. The absorption curves obtained for 1,3-cyclohexadiene in the vapor state in two different experiments are shown in Fig. 2. From Fig. 1 it can be seen that the absorption spectra of 1,3-cyclohexadiene in hexane and in alcohol coincide completely.

Both the spectra of the vapors and of 1,3-cyclohexadiene solutions have only one maximum, which lies at λ 250.5 mμ (log ϵ 3.73) for the vapors and at λ 258 mμ (log ϵ 4.00) for 1,3-cyclohexadiene in solution. From Fig. 2 it can be seen that the data obtained in two different experiments for the absorption spectrum of the vapors are in complete agreement, which indicates a good reproducibility of the results. As a result, contrary to existing literature data, the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region has only one maximum.

SUMMARY

Contrary to existing literature data, the absorption spectrum of 1,3-cyclohexadiene in the ultraviolet region (220-300 mμ) has only one absorption maximum, found at 250.5 mμ (log ϵ 3.73) for 1,3-cyclohexadiene vapors and at λ 258 mμ (log ϵ 4.00) for solutions of 1,3-cyclohexadiene in hexane and alcohol.

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ISOTOPIC EXCHANGE OF SULFUR IN SALTS OF ORGANIC THIOSULFONIC ACIDS

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One of the most interesting characteristics of the isotopic exchange of sulfur is the unusual rapidity of the reaction between elemental sulfur and certain sulfur-containing salts. In contrast to oxygen compounds of the type of Na_2CO_3, Na_2SO_4, metal oxides, etc., practically not exchanging (at moderate temperatures) with molecular oxygen, the similar sulfur compounds: Na_2CS_3 [1], $Na_2S_2O_3$ [2], sulfides of the alkali metals [3], xanthates ROCSSNa [4] and dithiocarbamates $R_2NCSSNa$ [5], show exchange with elemental sulfur in solutions even in the cold. The behavior of these compounds in exchange reactions with elemental sulfur is quite different from the behavior of other organic sulfur-containing compounds of the type of R–S–R, R–S–S–R, $R_2C{=}S$, etc. In the majority of cases, the exchange proceeds with considerably greater ease in the first group of compounds than in the second.

TABLE 1

Compound	Formula	Sulfur (in %)	
		Found	Calculated
Sodium ethanethiosulfonate	$C_2H_5SO_2SNa$	43.8	43.2
Sodium benzenethiosulfonate	$C_6H_5SO_2SNa \cdot 1\frac{1}{2}H_2O$	28.8	28.6
Sodium p-toluenethiosulfonate	$CH_3C_6H_4SO_2SNa \cdot 2H_2O$	26.5	26.0
	$CH_3C_6H_4SO_2SNa$	30.0	30.4
Potassium p-toluenethiosulfonate	$CH_3C_6H_4SO_2SK$	27.9	28.3
Barium p-toluenethiosulfonate	$(CH_3C_6H_4SO_2S)_2Ba \cdot 5H_2O$	20.7	21.2
Sodium p-bromobenzenethiosulfonate	$BrC_6H_4SO_2SNa$	22.8	23.2
Sodium p-nitrobenzenethiosulfonate	$NO_2C_6H_4SO_2SNa$	26.0	26.5
Sodium p-aminobenzenethiosulfonate	$H_2NC_6H_4SO_2SNa$	26.4	25.9
Sodium α-naphthalenethiosulfonate	$C_{10}H_7SO_2SNa$	26.5	26.1
Sodium benzyl thiosulfate	$C_6H_5CH_2S{-}SO_3Na$	29.0	28.3
Sodium benzenesulfinate	$C_6H_5SO_2Na$	20.0	19.5

In a number of papers it was shown that the exchange reactivity of sulfur in sulfur-containing salts depends to a large degree on the nature of the metal. Exchange proceeds rapidly in the case of the dithiocarbamates and xanthates of sodium [5] and potassium [4], and only slowly at 120-180° in the case of the corresponding lead, zinc, bismuth and nickel salts [6-8]. It was shown [6] on the example of sodium dibutyldithiocarbamate that the rate and energy of activation of exchange with elemental sulfur depend on the polar properties of the solvent. The greater the dissociation capacity of the solvent, the more rapid is the isotopic exchange of sulfur. These facts serve as evidence that ions participate in the exchange reaction with elemental sulfur. One of the principal factors responsible for such a specific behavior of the indicated reactions is apparently the great ease with which the sulfur molecule is polarized by anions.

Our purpose in the present investigation was to make a more detailed study of the basic rules governing the exchange reactivity of sulfur in sulfur-containing salts, and also to elucidate the mechanism of the indicated exchange reactions.

As the object of study we selected a group of compounds that have remained unstudied in this respect up to now, namely the salts of various thiosulfonic acids, depicted by the formula $R-SO_2SMe$. Thiosulfonic acid derivatives find wide use in chemical practice as intermediates in the synthesis of dyes, pharmaceuticals, etc. For this reason a study of the mobility of the sulfur in these compounds is of great interest. We hoped to obtain some information on the influence exerted by certain factors, both purely structural – in order to determine the relationship existing between the structure and reactivity of the indicated compounds, as well as external factors like solvent and temperature, on the rate of isotopic exchange. We used the radioactive sulfur isotope S^{35} as the labeled atom.

Synthesis of purification of compounds used. The alkali metal salts of the thiosulfonic acids were synthesized by us from the corresponding sulfonyl chlorides RSO_2Cl and sulfides Me_2S by methods given in the literature [9]. The barium salt was obtained by precipitation of the sodium salt with barium chloride solution.

In most cases the compounds were purified by repeated recrystallization from alcohol. According to the literature, some of the salts under these conditions give crystallohydrates. To obtain anhydrous compounds we used anhydrous alcohol for recrystallization.

The compounds were identified by analyzing for sulfur by the Carius method. The analysis results of the investigated salts are given in Table 1.

The solvents used in our study were dried and then distilled, taking the fractions with constants corresponding to those given in the literature.

TABLE 2

Salt	Activity of original sulfur (impulses/min)	Activity of salt after exchange	Calculated activity of salt in the case of exchange	
			of one sulfur atom	of two sulfur atoms
Sodium p-toluenethiosulfonate	2630	638	657	876
Potassium p-toluenethiosulfonate	6142	1533	1535	2047
Sodium ethanethiosulfonate	1306	324	326	435
Sodium p-bromobenzenethiosulfonate	1600	391	400	533

Isotopic exchange of sulfur in salts of thiosulfonic acids. By analogy with the exchange of sulfur in sodium thiosulfate $NaO-SO_2SNa$ [10], it could be expected that in the organic thiosulfonates of the alkali metals, RSO_2SNa, only the bivalent sulfur atom not linked to the radical R will also be capable of exchange reaction. To verify this we performed some experiments on the exchange of sulfur between salts of thiosulfonic acids with various R radicals, on the one hand, and elemental radioactive sulfur on the other. The experiments were run in 0.1N solutions with the ratio of the components 1 mole of salt : 1 atom of sulfur. In view of the fact that the investigated salts are most easily dissolved in polar solvents, and sulfur most easily in nonpolar solvents, we used a toluene-alcohol mixture (1:1.5 by volume) as the solvent.

The specimens for determining the activity of the components after exchange were prepared as benzidine sulfate precipitates, the elemental sulfur of which and of the salt after isolation were oxidized by the Carius method.

The results of these experiments for the equilibrium state of the system are given in Table 2, where the calculated values of the activity in the case of exchange of one and of two sulfur atoms are also given.

From a comparison of the data in Table 1 it is quite obvious that only one sulfur atom in salts of thiosulfonic acids is capable of exchange reaction, independent of the radical R.

Judging by the behavior of sodium thiosulfate in exchange reactions with elemental sulfur [10], and also taking into consideration the fact that sulfur in various valence states does not show exchange [3], it is possible to conclude that it is the bivalent sulfur atom in organic thiosulfates that exchanges.

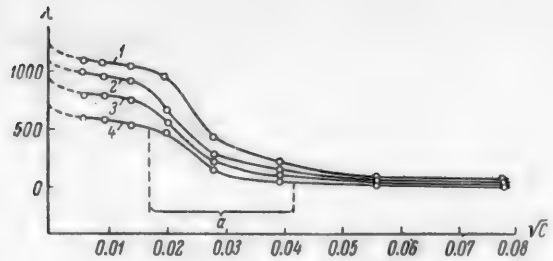

Fig. 1. Conductivity of $NH_2C_6H_4SO_2SNa$ (1), $CH_3C_6H_4SO_2SNa$ (2), $CH_3C_6H_4SO_2SK$ (3) and $NO_2C_6H_4SO_2SNa$ (4) as a function of the concentration.

TABLE 3

Exchange with Elemental Sulfur ($c_{salt} = c_{sulfur} = 0.1$ N in Toluene-Alcohol Mixture)

Expt. No.	Salt	Formula of substance after exchange	Temperature	K · 10⁴	E (kcal/mole)
1	Sodium ethanethiosulfonate	$C_2H_5SO_2S^*Na$	45°	0.279	16.6
			57	0.703	
			74	2.55	
2	Sodium benzenethiosulfonate	$C_6H_5SO_2S^*Na$	21	0.64	15.5
			32	1.66	
			52	8.60	
3	Sodium p-bromobenzenethiosulfonate	$BrC_6H_4SO_2S^*Na$	21	0.195	14.7
			41	1.0005	
			57	3.09	
4	Sodium p-nitrobenzenethiosulfonate	$NO_2C_6H_4SO_2S^*Na$	41	0.988	14.8
			50	1.92	
			60	4.16	
5	Sodium p-toluenethiosulfonate	$CH_3C_6H_4SO_2S^*Na \cdot 2H_2O$	20	0.60	14.8
			24	0.85	
			30	1.01	
			41	2.80	
6	Sodium α-naphthalenethiosulfonate	$C_{10}H_7SO_2S^*Na$	40	0.67	14.4
			55	2.00	
			65	4.51	
7	Sodium p-aminobenzenethiosulfonate	$H_2NC_6H_4SO_2S^*Na$	41	3.70	
8	Sodium p-toluenethiosulfonate	$CH_3C_6H_4SO_2S^*Na$	38.5	2.00	
9	Potassium p-toluenethiosulfonate	$CH_3C_6H_4SO_2S^*K$	38.5	0.40	
10	Barium p-toluenethiosulfonate	$(CH_3C_6H_4SO_2S^*)_2Ba \cdot 5H_2O$	44 (5 hrs)	No exchange	
			100 (5 hrs)		
			171 (5 hrs)		
11	Sodium benzyl thiosulfate	$C_6H_5CH_2S-SO_2-ONa$	100 (5 hrs)	No exchange	
			120 (5 hrs)		
			190 (5 hrs)		

TABLE 4

Compound	Degree of dissociation at 15° (in %)			
	0.05 N	0.0125 N	0.0031 N	0.00018 N
Sodium p-aminobenzenethiosulfonate	4	6	14	100
Sodium p-toluenethiosulfonate	3	4	12	100
Sodium benzenethiosulfonate	3	4	12	100
Potassium p-toluenethiosulfonate	2	3	6	100
Sodium p-nitrobenzenethiosulfonate	3	5	6	80

In order to determine the influence exerted by the structure of the radical R and the nature of the metal on the mobility of the sulfur in these compounds, and also to answer some of the questions on the mechanism of the exchange reaction, we quantitatively measured the exchange rate.

The experiments made to measure the kinetics of the exchange of sulfur between a given salt and elemental sulfur were run in toluene-alcohol solvent (1:1.5) and, depending on the experiment temperature, either in a special apparatus [11] or in sealed ampuls in a thermostat. In all of the experiments we took 0.1 N solutions, with the ratio of the components equal to 1 mole of salt : 1 atom of sulfur. The course of the exchange reaction was followed by the change in the activity of the salt. The latter was extracted from the reaction mixture with water, isolated from the solution after evaporation, and purified by recrystallization from water. To determine the activity, the salt precipitatestaken were of maximum thickness (190-210 mg per 5 sq cm).

It was established in advance that exchange does not occur with such a method of operation.

We determined the isotopic exchange constants from the equation $K = -\frac{1}{t}\ln\ 1 - \frac{\chi}{\chi_\infty}$ expressing the relationship between the activity of the salt χ and the time t. The activation energy E was determined for some of the compounds from the values of K as a function of the temperature.

It should be mentioned that the temperature interval was small, only 30 to 40°, and that the accuracy of determining E was of the order 0.5-1 kcal.

The results of measuring the rate with which the sulfur in various salts of thiosulfonic acids exchanges with elemental sulfur are given in Table 3.

To answer the question as to the mechanism of the investigated exchange reactions it was essential to have some information on the dissociation of salts of thiosulfonic acids in a toluene-alcohol mixture.

We used the compensation method to measure the conductivity of a number of salt solutions at 15° and with the concentrations: C = 0.05, 0.025, 0.0125, 0.0062, 0.0031, 0.0015, 0.0007, 0.0003 and 0.0001N.

The results of the measurements are shown in Fig. 1, where the values of λ are plotted along the ordinate, and the values of $\sqrt{c}$ along the abscissa.

As can be seen, the curves $\lambda - \sqrt{c}$ have approximately the same shape for all of the compounds investigated. A sharp rise is present in the interval of $\sqrt{c}$ values ranging from 0.04 to 0.02 (region a). A smooth change in the conductivity is observed above and below these values of $\sqrt{c}$ and a linear relationship is maintained between λ and $\sqrt{c}$.

Such a shape for the $\lambda - \sqrt{c}$ curves is apparently due to the specific properties of the solvent used.

The degree of dissociation $\alpha = \frac{\lambda}{\lambda_\infty} 100$ shown by all of the investigated compounds rises sharply in the interval of solution concentrations ranging from 0.0015 to 0.0003N. Above and below this range of concentrations the degree of dissociation changes but slightly with dilution.

The degrees of dissociation shown by the investigated compounds at various concentrations, with the exception of region a, are given in Table 4.

TABLE 5

Reaction Rate of Sodium Benzensulfinate with Sulfur in 0.1N Alcohol-Toluene Solutions

Temperature	K · 10⁴	E (kcal/mole)
20°	0.66	15.4
30	1.55	
37	3.04	

TABLE 6

Compound	K · 10⁴
$H_2NC_6H_4SO_2SNa$	3.7
$C_6H_5SO_2SNa$	3.1
$CH_3C_6H_4SO_2SNa$	2.8
$BrC_6H_4SO_2SNa$	1.0
$NO_2C_6H_4SO_2SNa$	1.0
α-$C_{10}H_7SO_2SNa$	0.8
$C_2H_5SO_2SNa$	0.3

DISCUSSION OF RESULTS

As can be seen from the above material, 1 sulfur atom in the alkali metal salts of organic thiosulfonic acids is exceedingly labile and exchanges with elemental sulfur in 0.1N solutions at 20-40°. Such an atom is the bivalent peripheral sulfur atom in $R-SO_2-S^*Na$.

From a comparison of the data on the exchange reactivity of the sulfur in salts of various metals, sodium, potassium and barium (Table 3, Nos. 8-10), it is obvious that the nature of the metal exerts a very large influence on the mobility of the sulfur atom found in salts of thiosulfonic acids. With other conditions constant, the rate of sulfur exchange in potassium toluenethiosulfonate is 1/6 as fast as in the case of the corresponding sodium compound, while the barium derivative does not exchange with sulfur even at 170°. In this respect the behavior of the thiosulfonate derivatives is similar to that shown by dithiocarbamate [5, 6] and xanthate [4] compounds, where a large difference is also observed in the exchange-reactivity of sulfur as a function of the nature of the metal. What is the reason for such a marked difference in the behavior of the investigated compounds?

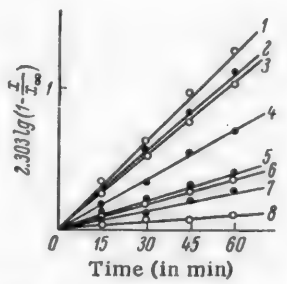

Fig. 2. Rate of exchange in the salts: $NH_2C_6H_4SO_2SNa$ (1), $C_6H_5SO_2SNa$ (2), $CH_3C_6H_4SO_2SNa$ (3), $(CH_3CO_2)_2NC_6H_4SO_2SNa$ (4), $BrC_6H_4SO_2SNa$ (5), $NO_2C_6H_4SO_2SNa$ (6), $C_{10}H_7SO_2SNa$ (7) and $C_2H_5SO_2SNa$ (8).

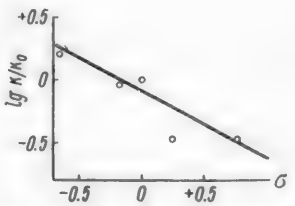

Fig. 3. Relationship between exchange velocity constants and Hammett values σ.

In discussing the exchange reactions of sulfur in the indicated salts, it is important to know the state of the elementary particles entering into exchange reaction with sulfur, i. e., whether they are salt molecules or ions.

On the basis of a number of facts and primarily on the basis of the data in [6] on the rate of sulfur exchange in sodium dibutyldithiocarbamate, which depends on the dissociation ability of the solvent (various mixtures of toluene + alcohol + water), it is possible to conclude that the principal factor, responsible for the rapid exchange shown by the above salt, is the presence of a suitable anion in solution, capable of exchange.

As regards the salts of thiosulfonic acids, it is also most probable to assume that exchange occurs with the participation of ions. If such is true, then a definite relationship should exist between the exchange capacity shown by the compounds and their degree of dissociation.

From a comparison of the data in Table 3, and also in Fig. 1, for the toluenethiosulfonates of sodium, potassium and barium it is quite obvious that both the exchange capacity and the degree of dissociation shown by these compounds changes in the order sodium > potassium ≫ barium.

Potassium toluenethiosulfonate is less dissociated in solution than is the corresponding sodium compound, and exchanges much more slowly. Solutions of barium toluenethiosulfonate are practically nonconductive; the compound does not dissociate into ions and does not exchange.

We found that the addition of a small amount of the sodium salt catalyzes the isotopic exchange of sulfur in the barium derivative. Thus, when the reaction between $(CH_3C_6H_4SO_2S)_2Ba$ and elemental sulfur S^{35} was run in the presence of $CH_3C_6H_4SO_2SNa$ (3% on the weight of barium salt) it was established that the exchange proceeds quite rapidly even at 43°.

In essence it is possible for two independent reactions to proceed in such a system – the exchange of sulfur between sodium toluenethiosulfonate and elemental sulfur and the exchange of $CH_3C_6H_4SO_2S$ groups between the sodium and barium salts.

$$CH_3C_6H_4SO_2S^- + S^* \rightleftarrows CH_3C_6H_4SO_2S^{*-} + S$$
$$CH_3C_6H_4SO_2S{-}Ba{-}SSO_2C_6H_4CH_3 + 2CH_3C_6H_4SO_2S^{*-} \rightleftarrows$$
$$\rightleftarrows CH_3C_6H_4SO_2S^*{-}Ba{-}S^*SO_2C_6H_4CH_3 + CH_3C_6H_4SO_2S^-$$

As a result of these two fairly rapid reactions a labeled sulfur atom appears in the barium salt. The accelerating effect of the sodium derivative reduces to a transfer of labeled $CH_3C_6H_4SO_2S^{*-}$ groups to the barium salt.

A similar mechanism for the catalytic action of the corresponding sodium derivative was convincingly demonstrated [6] in the case of the isotopic exchange of sulfur in nickel diethyldithiocarbamate and in thiuram.

As a result, the specific influence exerted by the nature of the metal (sodium, potassium, barium) on the ability of salts of thiosulfonic acids to exchange is manifested mainly through a variable ability of the corresponding compounds to dissociate into ions.

How can the appearance of a labeled sulfur atom in the corresponding thiosulfonic acid salt be depicted? Here several methods are possible. On the basis of a number of experimental facts we consider it most probable that the following reactions, leading to exchange, are present in the system:

$$1)\ RSO_2SNa \rightleftarrows RSO_2S^- + Na^+$$
$$2)\ RSO_2S^- + S_n \rightarrow RSO_2{-}S{-}S{-}S \ldots S^- \rightleftarrows RSO_2^- + S_{n+1}$$
$$3)\ RSO_2^- + Na^+ \rightleftarrows RSO_2Na$$
$$4)\ RSO_2^- + S_n^* \rightleftarrows RSO_2{-}S^*{-}S^*{-}S^* \ldots S^* \rightarrow RSO_2S^{*-} + S_{n-1}^*$$
$$5)\ RSO_2S^{*-} + Na^+ \rightleftarrows RSO_2S^*Na$$

The given scheme includes the formation of the sodium sulfinate as an intermediate product (2, 3), which then adds the labeled sulfur atom (4, 5).

To obtain proof for such a mechanism we attempted to study the individual stages of this reaction separately and evaluate the energy factors.

As regards the first stage, then here the dissociation of the investigated compounds into ions in the solvent used was shown by us experimentally; in this connection the values given in Table 4 refer to the conductivities of the solutions at 15°, and the salts show a much higher degree of dissociation at the temperatures at which the exchange experiments were run (20-70°).

The fact that sulfinic acid salts are formed (stages 2 and 3) in the reaction of thiosulfonic acid salts with sodium polysulfide and with sodium sulfite has been discussed in the literature [12]. The fact that a sodium sulfinate is formed was confirmed by us by reacting labeled sodium toluenethiosulfonate with sodium sulfite in aqueous solution at 43°.

$$CH_3C_6H_4SO_2S^*Na + Na_2SO_3 \rightarrow CH_3C_6H_4SO_2Na + Na_2S^*SO_3$$

The products isolated from this reaction were sodium toluenesulfinate (with a sulfur content of 17.3% after recrystallization from alcohol; calculated 17.9%), which did not contain any labeled sulfur atoms, and labeled sodium thiosulfate.

The reaction of a sodium sulfinate with elemental sulfur (stages 4 and 5) was studied by us on the example of reacting sodium benzenesulfinate with radioactive sulfur.

The kinetics of the reaction $C_6H_5SO_2Na + S^* \rightarrow C_6H_5SO_2S^*Na$ in toluene-alcohol medium (1:1.5) was measured by us at various temperatures.

The formation rate of the sodium benzenethiosulfonate was determined by quantitative analysis of the product obtained from the reaction mixture. The product was extracted from the reaction mixture with water, and then isolated from the solution after evaporation.

The results are summarized in Table 5.

Quite noteworthy is the fact that the velocity constants for the exchange of sulfur in sodium benzenethiosulfonate at the given temperatures (Table 3, No. 2) are close in value to the velocity constants for the addition of sulfur to sodium benzenesulfinate (Table 5). The energy of activation is the same for both reactions: 15.4 and 15.5 kcal/mole.

We believe that the presented material is quite adequate to justify the conclusion that the above proposed mechanism for the exchange of sulfur in salts of organic thiosulfonic acids is valid.

It should be mentioned that in principle this reaction scheme is analogous to the extensively studied [13] reaction for the exchange of sulfur between sodium thiosulfate and labeled sodium sulfite

$$S_2O_3^{=} + S^*O_3^{=} \rightleftarrows SO_3^{=} + SS^*O_3^{=}$$

The difference consists in that in the first case the sulfur atom is transferred from the thiosulfonate ion to the sulfur molecule, and in the second case it is transferred to the sulfite ion. The activation energies for the two reactions are close: 14.5 kcal [13] for the thiosulfate-sulfite exchange, and 14-16 kcal for the compounds studied by us.

Apparently, the exchange between elemental sulfur and alkali metal polysulfides also proceeds by a similar scheme of successive acts of transfer and addition of the sulfur atom. The difference consists in that in the polysulfides, together with exchange, there is sulfur addition with the formation of higher polysulfides, while in the case of the thiosulfonic acid salts such addition is not observed, probably due to the instability of such polysulfide compounds.

The sulfur molecule S_8 becomes reactive in the presence of suitable sulfur-containing anions in solution, and easily adds sulfur atoms. The principal reason for sulfur behaving in this manner is probably due to the polarizing action exerted by the anion on the sulfur molecule, leading to rupture of the ring.

From the data in Table 3 it can be seen that the exchange capacity shown by thiosulfonic acid salts is influenced not only by the nature of the metal atom, directly attached to the exchanging sulfur atom, but also by the composition and structure of the radical R. The energy of activation for exchange in the investigated compounds is small, and the influence exerted by the radical is manifested very poorly here.

However, this influence is quite distinctly manifested when the exchange rates are compared.

The velocity constants for exchange with an aliphatic radical (ethyl) are approximately 10 times smaller than the velocity constants for exchange with an aromatic radical like phenyl or tolyl.

For greater clarity we have plotted in Fig. 2 the values of $-\ln(1 - x/x_\infty)$ as a function of time, obtained for various compounds in solutions of constant concentration at 41°. The K values corresponding to these data are given in Table 6.

The influence exerted by the radical on the ability of the sulfur in thiosulfonic acid salts to exchange can

be manifested to varying degree in the different factors that determine the course of the reactions: stereochemistry of the reactions, degree of dissociation of the corresponding salts, magnitude of the effective charge on the exchanging sulfur atom in the anion of the thiosulfonic acid, etc.

In those cases where the radicals are quite different from each other, for example ethyl and naphthyl, the extent to which each of these factors is manifested can be different, and in order to establish any rules it is necessary to accumulate a much greater amount of experimental data than was obtained in the present study.

In the case where the radicals are close in composition and structure, for example substituted phenyls, the influence exerted on the ability to exchange is more uniform, and a comparison of the data for this type of compound is quite in order. From the data in Table 3 (and also Table 6) on the exchange of sulfur in various substituted sodium benzenethiosulfonate derivatives it can be seen that the introduction of electron-donor substituents (NH_2) in the para-position of the benzene ring facilitates exchange, while the introduction of electron-acceptor substituents (NO_2, Br) hinders exchange.

The principal factor responsible for the varying ability shown by the sulfur in this series of compounds to exchange is apparently the magnitude of the effective charge on the sulfur atom in the anion of the thiosulfonic acid. The larger the charge, the greater is the polarizing action on the sulfur molecule, and consequently the more probable is the formation of the complex. Electron-acceptor substituents reduce the magnitude of the effective charge, while electron-donor substituents increase it.

As a result, the reactions for the exchange of sulfur between thiosulfonic acid salts and elemental sulfur are heterolytic in nature.

As is known, the influence of substituents on the rate of such reactions obeys the Hammett rule.

We compared the values obtained by us for $\log (K/K_0)$, where K is the velocity constant for sulfur exchange in the substituted compound, and for exchange in the unsubstituted compound, with the Hammett values σ. The results are shown in Fig. 3. As can be seen, within the limits of experimental error, a linear relationship exists between $\log (K/K_0)$ and σ, with ρ equal to -0.56.

SUMMARY

1. The exchange of sulfur between various thiosulfonic acid salts RSO_2SMe and elemental sulfur S^{35} in toluene-alcohol solution was studied at various temperatures. The energy of activation of the exchange reactions was determined.

2. It was shown that both the radical and the metal exert considerable influence on the ability shown by the salts to exchange.

An analysis was given of the influence exerted by the composition and structure of the radicals on exchange.

3. The conductivity of a number of thiosulfonic acid salts in a toluene-alcohol mixture was measured at various salt concentrations. The degree of dissociation was determined.

4. A mechanism for the reaction of sulfur exchange in thiosulfonic acid salts was evolved.

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SYNTHESIS OF UNSYMMETRICAL DIALKYLHYDRAZINES

B. V. Ioffe

The most convenient method for the synthesis of unsymmetrical secondary hydrazines is the reduction of nitrosamines with a large excess of zinc dust in acetic acid medium [1-4]. Only the method for the preparation of dimethylhydrazine [4] has been developed in detail, but this same method has also been used to obtain both diethylhydrazine [1, 2] and (in somewhat lower yields) the simpler aromatic hydrazines [3]. An attempt [5] to synthesize mixed unsymmetrical aliphatic hydrazines (methylpropyl-, methylisobutyl- and methylisoamylhydrazines) by this method proved unsuccessful: reduction of the nitrosamines gave the corresponding secondary amines, and only once, when the reaction with methylisobutylnitrosamine was run in the cold did it prove possible to isolate a small amount of methylisobutylhydrazine as the methyl isobutylsemicarbazide. Unsatisfactory results were also obtained when this method was used to synthesize the dipropyl- and dibutylhydrazines [6], and reduction of the nitrosamines with aluminum lithium hydride has been recommended as a method for the preparation of these compounds [6, 7].

TABLE 1

Yields of Secondary Amines and Hydrazines in the Reduction of Nitrosamine with Zinc Amalgam in Hydrochloric Acid Medium

Nitrosamine	Yield (in mole %)	
	secondary amine	secondary hydrazine
Diethylnitrosamine	12	69
Methyl-n-propylnitrosamine	8	71
Methylisopropylnitrosamine	10	59
Methyl-n-butylnitrosamine	16	69
Methylisobutylnitrosamine	16	76
Di-n-propylnitrosamine	21	70
Di-n-butylnitrosamine	30	48
Methylphenylnitrosamine	71	0

Reduction with sodium in alcohol and with sodium in liquid ammonia in the presence of alcohol have also been proposed recently as methods for the preparation of hydrazines from nitrosamines [7].

In this communication we propose a method for the synthesis of unsymmetrical dialkylhydrazines, differing from previously described methods in its simplicity, lower consumption of reagents, and good yields of hydrazines. The method recommended by us is based on the reduction of nitrosamines with zinc amalgam in hydrochloric acid medium.

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!N{-}NO + 2Zn_{(Hg)} + 4HCl \longrightarrow 2ZnCl_2 + H_2O + \begin{matrix} R \\ R' \end{matrix}\!\!>\!N{-}NH_2 \qquad (1)$$

TABLE 2

Unsymmetrical Secondary Hydrazines, Obtained by the Reduction of Nitrosamines with Zinc Amalgam

Unsymmetrical hydrazines	Boiling point (pressure in mm)	d^{20}_4	$n^{20}D$	MR_D Found	MR_D Calculated*
Diethylhydrazine	98.0- 99.6° (756)	0.8004	1.4214	27.95	28.00
Methyl-n-propylhydrazine	103.2-103.7 (753)	0.7986	1.4208	27.98	28.00
Methylisopropylhydrazine	101.3-101.7 (769)	0.8096	1.4234	27.75	28.00
Methyl-n-butylhydrazine	128.0-128.2 (736)	0.8028	1.4267	32.66	32.65
Methylisobutylhydrazine	115.4-115.9 (758)	0.7930	1.4207	32.65	32.65
Di-n-propylhydrazine	141.0-142.2 (764)	0.8008	1.4270	37.26	37.30
Di-n-butylhydrazine	79.5- 81 (20)	0.8089	1.4347	46.51	46.59

The reduction is run by simply shaking the nitrosamine with dilute hydrochloric acid (1:1) and granulated zinc, covered with mercury. Due to the high hydrogen overvoltage on pure zinc amalgam the evolution of hydrogen fails to occur, and the reduction proceeds so rapidly and vigorously that it is necessary to cool the reaction mixture by the addition of ice.

The use of amalgam makes it possible to run the reaction in an ordinary separatory funnel and reduce the zinc consumption to the stoichiometric amount, i.e., to reduce the amount consumed to nearly 1/10 of that required with the Fischer method [1-4].

A secondary reaction in our method is the hydrolytic cleavage of the nitrosamines to secondary amine salts and nitrous acid

$$\begin{matrix} R \\ R' \end{matrix}\!\!>\!N\!-\!NO + H_2O + H^+ \longrightarrow \begin{matrix} R \\ R' \end{matrix}\!\!>\!NH_2^+ + HNO_2, \qquad (2)$$

which is then reduced further to ammonia [1, 2], nitric oxide and, possibly, in part to nitrous oxide.

The ratio of the yields of main and secondary products (hydrazines and amines) depends on the nature of the nitrosamines and the reaction conditions. Quantitative data on the yields of amines as secondary products of the reduction of nitrosamines have been nonexistent up to now. The analysis results obtained for the mixtures of bases, formed under the conditions recommended by us, are given in Table 1. As can be seen from these results, the role of the secondary reaction (2) increases with increase in the length of the hydrocarbon radicals. However, the yields of the dialkylhydrazines up to dibutylhydrazine remain excellent.

In attempting to use the described method to obtain the simplest aryl alkyhydrazine, unsym.-methylphenylhydrazine, it was found that the nitroso group is eliminated completely and the product obtained is pure N-methylaniline. Evidently, due to the great ease with which aromatic nitrosamines are hydrolyzed, the recommended method is not suitable for the synthesis of hydrazines with aromatic radicals.

The homologs of unsym.-dimethylhydrazine have been studied but slightly up to now.

The seven unsymmetrical aliphatic hydrazines synthesized in this paper were characterized by determining their physical constants (see Table 2), in which connection three of them are new (methyl-n-propyl-, methylisopropyl- and methylisobutylhydrazine). The new homologs of unsym.-dimethylhydrazine are colorless liquids with a characteristic odor, differing from the odor of amines, readily soluble in water and, using methyl orange as indicator, titrate as monoacidic bases in aqueous solution.

EXPERIMENTAL**

Synthesis of nitrosamines. Dimethylnitrosamine was obtained by the distillation of a mixture of concentrated

* Using the bond refractions of Vogel (see [6] and [11], p. 182).

** Student L. E. Poroshina assisted in the work.

TABLE 3

Properties of Nitrosamines Used for the Synthesis of Unsymmetrical Secondary Hydrazines

Nitrosamines	Boiling point at 40 mm	d^{20}_4	$n^{20}D$
Dimethylnitrosamine	67.1-67.2°	1.0048	1.4368
Diethylnitrosamine	86.7-86.8	0.9424	1.4386
Di-n-propylnitrosamine	113.2	0.9153	1.4440
Di-n-butylnitrosamine	118-118.3 (15 mm)	0.8997	1.4478
Methyl-n-propylnitrosamine	90.4-91.2	0.9454	1.4414
Methylisopropylnitrosamine	87.6-87.9	0.9452	1.4402
Methyl-n-butylnitrosamine	107.1-107.7	0.9298	1.4443
Methylisobutylnitrosamine	99.7	0.9244	1.4420
Methylphenylnitrosamine	132-134 (22 mm)	1.1282	1.5777

dimethylamine hydrochloride and sodium nitrite (taken in slight excess) solutions, followed by salting out of the distillate with potash [8]. To remove amine impurities the salted out organic layer was shaken for a short time with potassium bisulfate, then dried over potash, and distilled through a column (12 theoretical plates). The yield of product, with the constants given in Table 3, was 76%.

Diethylnitrosamine was obtained in a similar manner in 74% yield.

For the difficultly water-soluble nitrosamines with larger radicals it is expedient to use the method described below, not requiring distillation of the reaction mixture.

One gram-mole of ice-cooled secondary amine was added in small portions with stirring to a cooled mixture of 87 ml of concentrated hydrochloric acid (d 1.18) and 115 ml of water. To the obtained solution was added 76 g (1.1 g-mole) of sodium nitrite and the mixture was boiled under reflux for 40-60 minutes. The yellow layer of nitrosamine was separated, dried over potash, and fractionated through a column at 40 mm. The yields of pure nitrosamines by this method ranged from 87 to 91%.

Methylphenylnitrosamine was synthesized from technical methylaniline by the method of Hartman and Roll [9].

Reduction of nitrosamines with zinc amalgam. Into a 2.5-liter separatory funnel was placed 132 g (2.02 g-atom) of granulated zinc (arsenic-free) and 15 ml of mercury. Then 0.5 kg of ice was added, after which 450 ml of concentrated hydrochloric acid (d 1.18) was added gradually, with slight shaking of the funnel so that the surface of the zinc remained covered by the mercury and hydrogen was not evolved. Then 1 g-mole of the nitrosamine was added in portions. Approximately one third of the total nitrosamine was added at the start and the mixture shaken vigorously until heat was no longer evolved. The remaining nitrosamine was added in several portions, at the same time adding ice (another 0.5 kg in portions) to the reaction mixture. After each addition of nitrosamine and ice the mixture was shaken vigorously until reaction ceased. The amounts of nitrosamine added, the addition of ice, and the vigor of shaking, were regulated in such manner that the temperature in the funnel did not rise too high (up to 60°) and the funnel could be handled manually.

When all of the nitrosamine had been added the vigorous shaking was continued until heat was no longer evolved, the odor of the nitrosamine had disappeared, and nearly all of the zinc granules had dissolved.

The total time required to run the reaction with the indicated amounts of reactants is about 3/4 hour. The mercury layer is separated and can be used in subsequent experiments. The water layer is mixed with 300 ml of 50% sodium hydroxide solution in a three-liter round-bottomed flask. The flask is then connected through a spray catcher to a descending condenser and the volatile bases are steam-distilled.

The optimum amounts of distillate and alkali for salting out are indicated below for each compound.

The organic bases, salted out from the distillate with sodium hydroxide, after drying over solid caustic were distilled through a Vigreux column with a rated efficiency of 15 theoretical plates. The receivers were

protected from atmospheric moisture and carbon dioxide by a soda lime tube.

The first fractions represent secondary reduction products – the secondary amines, and the last fractions represent the hydrazines. Small amounts of water, usually present despite the drying over caustic, distill either as minimum azeotropes with the amines, provided the boiling points of the latter are close to 100°, or with the hydrazines. In the latter case the pure hydrazine fraction precedes the water-containing hydrazine fraction, having higher density and refractive index values.

The yields of amines and hydrazines given in Table 1 were calculated from the analysis data obtained in the titration of the fractions and residue with 0.1N hydrochloric acid, using methyl orange as indicator. Small intermediate fractions were considered to be binary mixtures of amine and hydrazine and were analyzed by refractive index.

Unsym.-diethylhydrazine. After the reduction of 102 g of diethylnitrosamine under the above described conditions we took 300 ml of the aqueous distillate and added 120 g of sodium hydroxide to it with cooling. The separated layer of 78.4 g of organic bases was dried over solid sodium hydroxide and then distilled through the column at 756 mm. The following fractions were obtained:

1st, 52-57.5°, 8.2 g, d^{20}_4 0.7074, $n^{20}D$ 1.3848 (diethylamine).

Pure diethylamine, according to our data, has b. p. 56.1-56.2° at 776 mm, d^{20}_4 0.7053, $n^{20}D$ 1.3850.

2nd, 57.5-88°, 1.3 g, $n^{20}D$ 1.4006 – mixture of amine and hydrazine (with a small amount of water). Amount of amine, based on $n^{20}D$, 58%.

3rd, 88-98°, 6.2 g, $n^{20}D$ 1.4224 – diethylhydrazine with water as impurity. Diethylhydrazine content 88.3%.

4th, 98-99.6°, 53 g, d^{20}_4 0.8004, $n^{20}D$ 1.4214 – unsym.-diethylhydrazine. Yield 60.2%. Literature for unsym diethylhydrazine [6]: b. p. 99.5-100° at 762 mm, d^{20}_4 0.7988, $n^{20}D$ 1.42136.

Residue, 6.4 g, $n^{20}D$ 1.4330. Diethylhydrazine content 41.9%. Partially soluble in water. The water-insoluble yellow layer after washing and drying over potash had $n^{20}D$ 1.4443 (diethylnitrosamine).

Unsym.-di-n-propylhydrazine. For reduction we took 97.7 g (0.75 g-mole) of di-n-propylnitrosamine and correspondingly smaller amounts of the other reactants. For salting out 200 ml of distillate we used 70 g of sodium hydroxide. The salted out organic layer after drying was fractionally distilled to give 53.2 g (61%) of di-n-propylhydrazine:

B. p. 141.0-142.2° (at 764 mm), d^{20}_4 0.8008, $n^{20}D$ 1.4270. Literature [6]: b. p. 140.5-141° (768 mm), 31.5° (7 mm), d^{20}_4 0.7997, $n^{20}D$ 1.42661.

When an acetic acid solution of the dipropylhydrazine was heated with concentrated potassium cyanate solution we obtained 1,1-di-n-propylsemicarbazide, which after recrystallization from dilute alcohol (1:1) had m. p. 114-115°. Literature [7]: m. p. 116°.

The intermediate fraction with b. p. 111-141° and the distillation residue contained (based on the analysis data) another 7.4 g of the di-n-propylhydrazine.

As a secondary product of the reduction we obtained 9.7 g (12.8%) of di-n-propylamine: b. p. 108-111° (764 mm), d^{20}_4 0.7414, $n^{20}D$ 1.4052.

Pure di-n-propylamine has, according to our data, b. p. 108.7-108.9° (751 mm), d^{20}_4 0.7378, $n^{20}D$ 1.4042.

Another 6.2 g of di-n-propylamine was contained in the first (up to 108°) and intermediate (111-141°) fractions.

Unsym.-di-n-butylhydrazine. In the reduction of 62.6 g (0.4 g-mole) of di-n-butylnitrosamine we observed a weaker evolution of heat than in the case of the nitrosamines with smaller radicals, and here 15 g of unreacted zinc remained. The reaction mixture at the end of reduction was still heterogeneous; the organic layer congealed to a crystalline mass.

We removed 200 ml of the heterogeneous distillate. The water layer was salted out with 80 g of sodium

hydroxide. After drying over solid caustic the organic layer was distilled through the column at 20 mm: 1st fraction with b. p. 58.5-62° (11.1 g) was di-n-butylamine (d^{20}_4 0.7626, $n^{20}D$ 1.4182); 2nd fraction with b. p. 62-72.5° (7.7 g) was an intermediate fraction ($n^{20}D$ 1.4264); 3rd fraction (21.4 g, 37.4%) was pure di-n-butylhydrazine:

B. p. 79.5-81° (20 mm), d^{20}_4 0.8089, $n^{20}D$ 1.4347.

Found: equiv. weight 143.4, 144.7. $(C_4H_9)_2N_2H_2$. Calculated: equiv. weight 144.3.

Literature [6]: B. p. 61° (8 mm), d^{20}_4 0.8078, $n^{20}D$ 1.43430.

The 1,1-di-n-butylsemicarbazide obtained from the 3rd fraction had m. p. 92° (from 50% alcohol). Literature [7]: m. p. 94°.

The distillation residue (5.3 g) contained another 2.4 g of di-n-butylhydrazine.

Unsym.-methyl-n-propylhydrazine. After the reduction of 45.9 g (0.45 g-mole) of methyl-n-propylnitrosamine we removed 250 ml of alkaline distillate, which was saturated with sodium hydroxide (110 g). We obtained 7.3 g of wet 96.5% methyl-n-propylhydrazine (b. p. 96.7-103.2°, d^{20}_4 0.8044, $n^{20}D$ 1.4214) and 15.9 g (40.1%) of pure methyl-n-propylhydrazine with the following constants:

B. p. 103.2-103.7° (753 mm), d^{20}_4 0.7986, $n^{20}D$ 1.4208.

Found: equiv. weight 88.7, 89.7. $C_4H_{10}N_2H_2$. Calculated: equiv. weight 88.15.

Methyl-n-propylhydrazine is not described in the literature.

The distillation residue (4.5 g) and intermediate fraction with b. p. 63-96.7° (1.8 g, $n^{20}D$ 1.4120) contained another 5.3 g of methylpropylhydrazine.

The first fraction (2.1 g) was methyl-n-propylamine:

B. p. 60.3-63° (753 mm), d^{20}_4 0.7179, $n^{20}D$ 1.3907.

Found: equiv. weight 74.2, 74.3. $C_4H_{11}N$. Calculated: equiv. weight 73.14.

Unsym.-methylisopropylhydrazine. From 102 g (1 g-mole) of methylisopropylnitrosamine we obtained 500 ml of alkaline distillate, which was salted out with 280 g of sodium hydroxide.

The yield of the fraction corresponding to pure methylisopropylhydrazine was 35 g (39.8%):

B. p. 101.3-101.7° (769 mm), d^{20}_4 0.8096, $n^{20}D$ 1.4234.

Found: equiv. weight 85.2, 86.5. $C_4H_{10}N_2H_2$. Calculated: equiv. weight 88.15.

Unsym.-methylisopropylhydrazine is not described in the literature.

In addition, we obtained 13.1 g of a fraction with b. p. 93.8-101.3° (d^{20}_4 0.8346, $n^{20}D$ 1.4254), which was wet methylisopropylhydrazine, analyzed as 96% pure hydrazine. Another 4.37 g of methylisopropylhydrazine was contained in the intermediate fraction with b. p. 52-93.8° (3 g, $n^{20}D$ 1.4069) and distillation residue.

We obtained 5.9 g of the 1st (amine) fraction: b. p. 50.2-52° (769 mm), d^{20}_4 0.7042, $n^{20}D$ 1.3842, equiv. weight 73.8. The constants of this fraction are in complete agreement with those of methylisopropylamine.

Unsym.-methyl-n-butylhydrazine. For reaction we took 87 g (0.75 g-mole) of the nitrosamine. The distillate (250 ml) was salted out with 80 g of sodium hydroxide. On distillation we obtained 46.9 g (61.3%) of pure methyl-n-butylhydrazine:

B. p. 128-128.2° (736 mm), d^{20}_4 0.8028, $n^{20}D$ 1.4267.

Found: equiv. weight 102.5, 103.0. $C_6H_{12}N_2H_2$. Calculated: equiv. weight 102.2.

Literature [10]: B. p. 50.5-51° (38 mm), $d^{21.2}_4$ 0.8040, $n^{21.2}D$ 1.42586.

The intermediate fraction with b. p. 93-128° (4.8 g, $n^{20}D$ 1.4176) and the residue contained another 5.9 g of methyl-n-butylhydrazine.

The first fractions with b. p. 80.93° (7.7 g) were wet methyl-n-butylamine and contained 7 g of the amine

Unsym-methylisobutylhydrazine. For reduction we took 48.8 g (0.42 g-mole) of the nitrosamine. The alkaline distillate (140 ml) was salted out with 45 g of sodium hydroxide. Fractional distillation of the mixed bases gave 22.9 g (53.5%) of methylisobutylhydrazine:

B. p. 115.4-115.9° (758 mm), d^{20}_4 0.7930, $n^{20}D$ 1.4207.

Found: equiv. weight 102.8, 102.4. $C_5H_{12}N_2H_2$. Calculated: equiv. weight 102.2.

Unsym-methylisobutylhydrazine is not described in the literature.

1-Methyl-1-isobutylsemicarbazide: m. p. 110.5-111.4°.

Found %: N 28.79, 28.90. $C_6H_{15}ON_3$. Calculated %: N 28.93.

Literature [5]: m. p. 99°.

The intermediate fraction with b. p. 83-115.4° (7.4 g, $n^{20}D$ 1.4147) and the distillation residue (5 g) contained another 9.6 g methylisobutylhydrazine.

The 1st fraction with b. p. 75.5-83° (1.2 g, d^{20}_4 0.7662, $n^{20}D$ 1.4008) was wet (89%) methylisobutylamine.

Dimethylhydrazine hydrochloride. Unsym-dimethylhydrazine, despite its low boiling point, slowly distilled from the alkaline reaction mixture, probably due to formation of the hydrate. Salting out of the obtained dilute distillate with alkali (as in the above described syntheses) is not practical.

After the reduction of 74.1 g (1 g-mole) of dimethylnitrosamine the 600 ml of obtained distillate was neutralized (to methyl red) with 64.2 ml of concentrated hydrochloric acid. The solution was evaporated on the water bath, and the residue was dried in an oven for several hours at a temperature up to 120°. We obtained 74 g (77%) of the hydrochloride (see [4]).

The reduction of methylphenylnitrosamine was accompanied by a darkening of the reaction mixture and the formation of nitrogen oxides. The product was isolated in the usual manner and distilled completely at 90° (20 mm), did not reduce Fehling solution, and was pure methylaniline:

B. p. 195.3-196.1° (760 mm), d^{20}_4 0.9863, $n^{20}D$ 1.5712. Literature data for N-methylaniline [11]: b. p. 196.2° (760 mm), d^{20}_4 0.9862, $n^{20}D$ 1.5710.

From 102 g (0.75 g-mole) of methylphenylnitrosamine we obtained 57.3 g (71%) of methylaniline.

SUMMARY

1. A simple method for the synthesis of dialkylhydrazines was proposed, based on the reduction of nitrosamines with zinc amalgam in hydrochloric acid medium.

2. The following homologs of unsym-dimethylhydrazine were synthesized and characterized by determining their physical constants: diethylhydrazine, di-n-propylhydrazine, di-n-butylhydrazine, methyl-n-butylhydrazine, methylisobutylhydrazine, methyl-n-propylhydrazine and methylisopropylhydrazine. The last three compounds are new.

3. It was shown that increasing the length of the alkyl radicals leads to some reduction in the yield of hydrazines and a simultaneous increase in the yield of secondary products — the secondary amines.

Methylphenylnitrosamine under the indicated reduction conditions is converted to methylaniline.

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TETRAACYLOXYSILANES IN ORGANIC SYNTHESES

XIV.* SYNTHESIS OF HOMOLOGS OF CINNAMIC ACID (α-ALKYL-β-PHENYLACRYLIC ACIDS)

Iu. K. Iur'ev, G. B. Eliakov and A. N. Vysokosov

In a previous paper [1] we communicated that tetraacetoxysilane, the mixed anhydride of silicic and acetic acids, can successfully replace acetic anhydride in the synthesis of aromatic α,β-unsaturated acids by the Perkin reaction. Tetraacetoxysilane condenses with benzaldehyde in the presence of the conventionally used condensing agents – anhydrous potassium or sodium acetate, and also in the presence of potash, and here cinnamic acid is obtained in yields at least equal to those obtained with acetic anhydride.

In connection with this it seemed of great interest to investigate the possibility of utilizing the silicoanhydrides of other saturated monobasic organic acids to obtain homologs of cinnamic acid. In this paper we condensed the silicoanhydrides of propionic, butyric, valeric, isovaleric and caproic acids with benzaldehyde and obtained a number of α-alkyl-β-phenylacrylic acids in yields ranging from 29 to 69.5%.

$$2C_6H_5CHO + Si(OCOCH_2R)_4 \xrightarrow[K_2CO_3]{RCH_2COOK} \rightarrow 2C_6H_5CH{=}C(R){-}COOH + Si(OH)_4 + 2RCH_2COOH$$

(R = CH_3, C_2H_5, n-C_3H_7, n-C_4H_9).

When benzaldehyde was condensed with the silicoanhydrides of propionic, butyric and valeric acids under certain conditions we obtained only the corresponding α-alkylcinnamic acids, whereas in the case of using the silicoanhydride of isovaleric acid we obtained only the styrene homolog – 1-phenyl-3-methyl-1-butene in up to 70% yield. It should be mentioned that such a yield of 1-phenyl-3-methyl-1-butene is obtained only when the reaction is run under extremely drastic conditions (190-230°). However, it proves impossible to obtain α-isopropylcinnamic acid even under considerably milder conditions (100°, 20 hours of heating): a part of the benzaldehyde is recovered unchanged, and 1-phenyl-3-methyl-1-butene is the solitary reaction product, but its yield drops to 30%. From the literature it is known [2] that the main product in the condensation of benzaldehyde with the anhydride of isovaleric acid is also 1-phenyl-3-methyl-1-butene, together with the formation of only small amounts of α-isopropylcinnamic acid.

When the silicoanhydrides of butyric and caproic acids were condensed with benzaldehyde the corresponding styrene homologs – 1-phenyl-1-butene and 1-phenyl-1-hexene were formed as secondary reaction products (8.5-23%) in those cases where higher temperatures and a long heating time were employed.

The unsaturated hydrocarbon is formed together with the substituted cinnamic acid also when the anhydrides of the acids are used. Thus, 1-phenyl-2-methyl-1-propene [3] is formed when a mixture of isobutyric anhydride and benzaldehyde is heated in the presence of sodium isobutyrate at 150°. Its formation is explained as due to the decarboxylation of the intermediate addition product of the acid anhydride to benzaldehyde [4], since the α-isoalkylcinnamic acids as such are stable when heated above 100°.

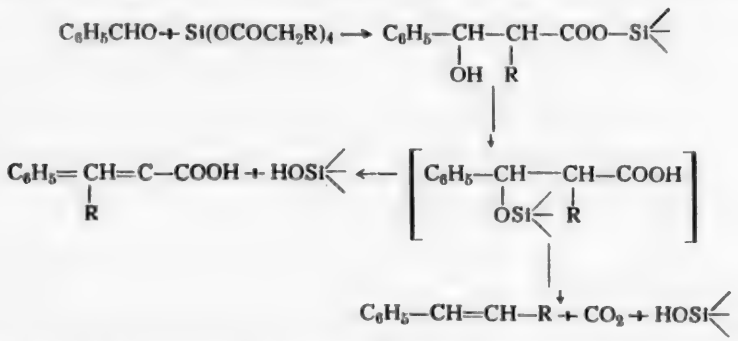
α-Isobutylcinnamic acid was obtained by the condensation of benzaldehyde with either sodium or potassium isocaproate and acetic anhydride [5]. At the same time the reaction of isovaleric anhydride with benzaldehyde

* For XI see J. Gen. Chem. 26, 926 (1956); for XII see Bull. Moscow State Univ., Phys. Chem. Series No. 1, 197 (1956).

in the presence of sodium isovalerate gives α-isopropylcinnamic acid in very poor yield (7%) [2], since here carbon dioxide is evolved from the reaction mixture even at 70°, and 1-phenyl-3-methyl-1-butene is obtained as the main product.

The formation of 1-phenyl-3-methyl-1-butene in the condensation of the silicoanhydride of isovaleric acid with benzaldehyde must also be attributed to decarboxylation of the intermediate addition product of the silicoanhydride of the organic acid to benzaldehyde.

In this connection a more probable (than that given earlier [1]) scheme for the condensation of a tetraacyloxysilane with benzaldehyde should be regarded to be that scheme which includes the intermediate formation of their addition product, with its subsequent isomerization to the ester of orthosilicic acid and α-alkyl-β-phenyl-β-hydroxyhydracrylic acid, which cleaving only the silicic acid yields the α-alkyl-β-phenylacrylic acid, and the styrene homolog when both decarboxylation and cleavage of the silicic acid occur:



Consequently, also in the formation of secondary reaction products the silicoanhydrides of saturated monobasic organic acids behave in the Perkin reaction in exactly the same manner as do the corresponding anhydrides. As a result, each case involving the condensation of silicoanhydrides of various organic acids with benzaldehyde requires its own reaction conditions (ratio of reactants, temperature and time of heating), in which connection higher yields of α-alkylcinnamic acids are obtained in the presence of the potassium salt of the acid found in the silicoanhydride than in the presence of potash (respectively 68% and 53% in the preparation of α-ethylcinnamic acid, and 36% and 22% in the preparation of α-n-butylcinnamic acid).

EXPERIMENTAL

To prepare the silicoanhydrides of the organic acids we charged 4 g-moles of the acid into a 500-ml round-bottomed flask fitted with reflux condenser and calcium chloride tube, then added 1.1-1.15 g-moles of silicon tetrachloride, mixed, and allowed to stand for 1-2 hours at 20°. Then the mixture was heated, at first on the water bath, and then with a low flame until the evolution of hydrogen chloride, which should proceed uniformly and not too vigorously, had ceased completely. Complete removal of the hydrogen chloride can be achieved by passing a stream of dry air through the hot silicoanhydride.

On cooling, the silicoanhydride was obtained at times as a solid mass (silicocaproic anhydride solidified even while hot), and at times as a gel, which was used as such to synthesize the α-alkylcinnamic acids [1].

Method of operation. In a 100-ml round-bottomed flask, fitted with reflux condenser and a stirrer descending through the condenser, was placed 0.1-0.2 g-mole of benzaldehyde and correspondingly 0.1-0.24 g-mole of the tetraacyloxysilane and 0.1-0.2 g-mole of either anhydrous potash or anhydrous potassium salt of the acid found in the tetraacyloxysilane. The mixture was mixed thoroughly and heated in an oil bath with constant stirring. If the reaction mixture solidified at the start, then the temperature was raised in several minutes to 20-30° above that chosen.

On conclusion of reaction the mass was cooled, treated with warm 2N sodium hydroxide solution until weakly alkaline (to litmus),* and the unchanged benzaldehyde steam-distilled. The residue in the flask was treated with activated carbon, boiled, steam passed through for 5 minutes, and then suction-filtered hot. The

* An excess of caustic should be avoided to prevent contamination of the reaction product with silicic acid.

precipitate on the filter was washed twice with small portions of 2N sodium hydroxide solution, then with warm water, and the acid was isolated from the combined filtrates by acidification with concentrated hydrochloric acid. The α-alkylcinnamic acids were usually obtained quite pure; they were recrystallized from anhydrous alcohol.

To isolate the styrene homolog, the distillate from the steam-distillation was saturated with common salt and then extracted with ether. The ether extract was washed with sodium bisulfite, then with alkali, and dried over calcium chloride. After removal of the ether by distillation the hydrocarbon was vacuum-distilled.

α-Methylcinnamic acid. A mixture of 10.6 g of benzaldehyde, 44 g of silicopropionic anhydride and 13.8 g of potash was heated for 12 hours at 190-195°. We obtained 11.2 g (69.5%) of α-methylcinnamic acid with m. p. 81-81.2°.

Found %: C 74.14, 74.20; H 6.25, 6.28. $C_{10}H_{10}O_2$. Calculated %: C 74.05; H 6.21.

Literature: m. p. 81° or 74° (due to the existence of two crystalline modifications) [6].

α-Ethylcinnamic acid. a) A mixture of 10.6 g of benzaldehyde, 37.6 g of silicobutyric anhydride and 13.8 g of potash was heated for 14 hours at 160-170°. We obtained 9.3 g (53%) of α-ethylcinnamic acid with m. p. 106°.

Found %: C 75.30, 75.32; H 7.08; 7.05. $C_{11}H_{12}O_2$. Calculated %: C 74.97; H 6.86.

Literature: m. p. 104° [6], 104-105° [7].

We also isolated 1.9 g (14.5%) of 1-phenyl-1-butene: b. p. 84-85° (20 mm), $n^{20}D$ 1.5384, d^{20}_4 0.9099, MR_D 45.46. $C_{10}H_{12}F_4$. Calculated 44.31.

Literature: b. p. 77° (10 mm), $n^{20}D$ 1.5387, d^{20}_4 0.9106 [8]; b. p. 89-90° (15 mm), $n^{16}D$ 1.5414, d^{16}_4 0.9124 [9]. 1-Phenyl-1,2-dibromobutane, obtained by reaction with bromine in chloroform, melted at 70°.

Found %: Br 54.64, 54.55. $C_{10}H_{12}Br_{12}$. Calculated %: Br 54.73.

Literature: m. p. 70° [10]; 71° [11].

b) The heating of a mixture of 36.8 g of silicobutyric anhydride, 10.6 g of benzaldehyde and 13.8 g of potash for 5 hours at 185-190° gave 8.4 g (48%) of α-ethylcinnamic acid with m. p. 106°, and 2.7 g (20%) of 1-phenyl-1-butene with b. p. 65-67° (7 mm) and $n^{20}D$ 1.5386.

c) The heating of a mixture of 10.6 g of benzaldehyde, 37.6 g of silicobutyric anhydride and 12.6 g of potassium butyrate gave 11.9 g (68%) of α-ethylcinnamic acid; m. p. 106°. The mixed melting point with the acid obtained from the preceding experiments was not depressed.

α-Propylcinnamic acid. A mixture of 10.6 g of benzaldehyde, 34.5 g of silicovaleric anhydride and 13.8 g of potash was heated for 5.5 hours at 185-190°. We obtained 5.5 g (29%) of α-propylcinnamic acid with m. p. 92.8-93°.

Found %: C 76.04, 76.02; H 7.52, 7.64. $C_{12}H_{14}O_2$. Calculated %: C 75.76; H 7.41.

Literature: m. p. 93° [12].

As shown in the preceding series of experiments, there is no doubt but that both a reduction in the temperature and an increase in the time of heating should favor an increase in the yield of acid.

1-Phenyl-3-methyl-1-butene. A mixture of 10.6 g of benzaldehyde, 64 g of silicovaleric anhydride and 13.8 g of potash was heated for 14 hours (9 hours at 190° and 5 hours at 230°). We obtained 10.42 g (70%) of 1-phenyl-3-methyl-1-butene.

B. p. 91-92.5° (17 mm), $n^{20}D$ 1.5228, d^{20}_4 0.8901, MR_D 50.17. $C_{11}H_{14}F_4$. Calculated 48.93.

Found %: C 90.21, 90.33; H 9.71, 9.69. $C_{11}H_{14}$. Calculated %: C 90.27; H 9.63.

Dibromide: m. p. 129-129.2°.

Found %: C 43.23, 43.35; H 4.69, 4.79; Br 51.99, 52.15. $C_{11}H_{14}Br_2$. Calculated %: C 43.17; H 4.61; Br 52.21.

Literature: b. p. 207° (757 mm); 102-103° (26 mm), $n^{14.6}D$ 1.5248, $d^{14.6}_4$ 0.8903 [9]; b. p. 94-105° (11 mm), $n^{20}D$ 1.5251, d^{20}_4 0.887 [13]; dibromide: m. p. 125° [10].

α-Butylcinnamic acid. a) A mixture of 10.6 g of benzaldehyde, 37.5 g of silicocaproic anhydride and 13.8 g of potash was heated for 10 hours at 160-165°. We obtained 4.5 g (22%) of α-butylcinnamic acid with m. p. 83.7°.

Found %: C 76.64, 76.61; H 8.07, 8.20. $C_{13}H_{16}O_2$. Calculated %: C 76.48; H 7.90.

Literature: m. p. 83-84° [4], m. p. 80° [12].

b) A mixture of 10.6 g of benzaldehyde, 48.9 g of silicocaproic anhydride and 19 g of potassium n-caproate was heated for 15 hours at 175-180°. We obtained 7.4 g (36%) of α-butylcinnamic acid; m. p. 83.5°.

The mixed melting point with the acid obtained from the preceding experiment was not depressed.

The secondary reaction product obtained here in 23% yield was a hydrocarbon fraction, which from its boiling point corresponded to 1-phenyl-1-pentene.

B. p. 116-121° (22 mm), $n^{20}D$ 1.5182, d^{20}_4 0.9028.

Literature: b. p. 82° (9 mm), d^{20}_4 0.892, $n^{15}D$ 1.5139 [14].

SUMMARY

1. It is possible to use the silicoanhydrides of aliphatic acids in place of the anhydrides of the corresponding acids in the condensation with benzaldehyde, leading to the formation of α-alkylcinnamic acids.

2. Only the corresponding cinnamic acids are obtained when the silicoanhydrides of propionic and valeric acids are employed; β-isopropylstyrene is the main reaction product when the silicoanhydride of isovaleric acid is utilized; together with α-alkylcinnamic acids, the corresponding styrenes are obtained as secondary reaction products when the silicoanhydrides of butyric and caproic acids are employed.

3. Higher yields of α-alkylcinnamic acids are obtained in the presence of the anhydrous potassium salt of the acid found in the silicoanhydride than in the presence of potash.

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TRANSAMINATION REACTIONS OF CARBOXYLIC ACID AMIDES

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An investigation of the reversible transamination of carboxylic acid amides, proceeding by the equation

$$RCONHR' + R''NH_2 \rightleftharpoons RCONHR'' + R'NH_2,$$

originated from the paper [1], where it was shown that transamination occurs when substituted ureas are reacted with primary amines, leading to the formation of a new substituted urea and a new amine

$$2NH_2R' + R''HNCONHR'' \rightleftharpoons 2NH_2R'' + R'HNCONHR'$$

Thus, for example, the reaction of N,N'-dipyridylurea with aniline gave N,N'-diphenylurea and aminopyridine. The indicated authors studied 7 pairs of a similar type of reversible reactions. To expand on this study we thought it would be interesting to investigate the transamination of carboxylic acid amides. First we studied the reaction of acetamide with aromatic amines and established that hydrogen chloride facilitates a shift in the equilibrium of this reversible reaction. For example, the heating of acetamide with aniline for 8 hours at 180-230° under the conditions described by Kelbe [2] yields a small amount of acetanilide, while in the presence of hydrogen chloride the same reaction leads to the quantitative formation of acetanilide in 45 minutes. When acetamide was reacted (in the presence of hydrogen chloride) with o-toluidine, and also with p-aminodimethylaniline, we obtained the corresponding acetyl derivatives in good yield, which makes the reaction of acetamide with aromatic amines a potentially useful method of acylation in certain cases.

A number of authors have attempted to react substituted amides with aromatic amines, but they were able to effect a shift of the equilibria of these reactions only under extremely drastic conditions. Thus, for example, a shift of the equilibrium of the reaction

$$CH_3CONHC_5H_{11} + RNH_2 \rightleftharpoons CH_3CONHR + C_5H_{11}NH_2$$

was achieved only by heating the reaction mixture for 2-5 days at 260° in dodecylpiperidine solution at a pressure of 100 atm [3].

The heating of acetanilide and p-anisidine for 13 hours gave aniline and p-acetanisidide, in which connection the presence of the p-acetanisidide was established spectrophotometrically [4].

We found that in the presence of hydrogen chloride the equilibrium of the reversible reaction

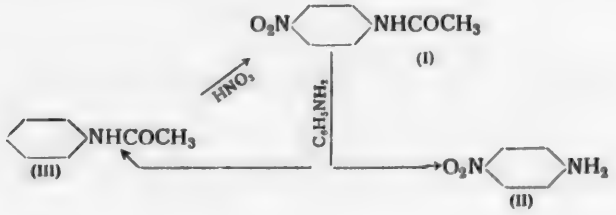
$$CH_3CONHR + R'NH_2 \rightleftharpoons CH_3CONHR' + RNH_2$$

is shifted in 45 minutes at 180-190° almost completely from left to right. We ran a number of transamination reactions, proceeding by the scheme

$$RNHCOCH_3 + R'NH_2 \rightleftharpoons R'NHCOCH_3 + RNH_2$$

In five of the reactions R' = C_6H_5, and R = o-$CH_3C_6H_4$, p-$(CH_3)_2NC_6H_4$, p-$CH_3OC_6H_4$, p-$CH_3C_6H_4$, p-$O_2NC_6H_4$; in one reaction R' = o-$CH_3C_6H_4$ and R = C_6H_5.

In all of these reactions we obtained the newly formed substituted amide and primary amine in nearly quantitative yield, which could be easily separated due to their different solubility in water. The reactions of aromatic amines with carboxylic acid amides can be used as a method for the simultaneous preparation of substituted amides and primary aromatic amines. Some of these reactions can be utilized in industry. For example, the reaction of p-nitroacetanilide with aniline can serve as a base for the commercial preparation of p-nitroaniline, operated as a cyclic process by the scheme



This process is economical for the reason that both the final reaction product, p-nitroaniline (II), and the starting product, acetanilide (III), which is used in the same cyclic process to obtain p-nitroaniline, are formed simultaneously at the stage of heating p-nitroacetanilide (I) with aniline. The advantage of the proposed method for obtaining p-nitroaniline over the present method of manufacture, proceeding in 3 stages by the scheme

$$C_6H_5NH_2 \xrightarrow{(CH_3CO)_2O} C_6H_5NHCOCH_3 \xrightarrow{HNO_3} p\text{-}O_2NC_6H_4NHCOCH_3 \xrightarrow{H_2SO_4} p\text{-}O_2NC_6H_4NH_2$$

consists in a reduction of the number of steps to two and a corresponding decrease in the consumption of aniline, acetic anhydride sulfuric acid and other raw materials. It is possible to obtain sulfanilamide (white streptocide) on a commercial scale by a similar scheme. The method used in the pharmaceutical industry at the present time to obtain sulfanilamide, proceeding in 4 stages by the scheme

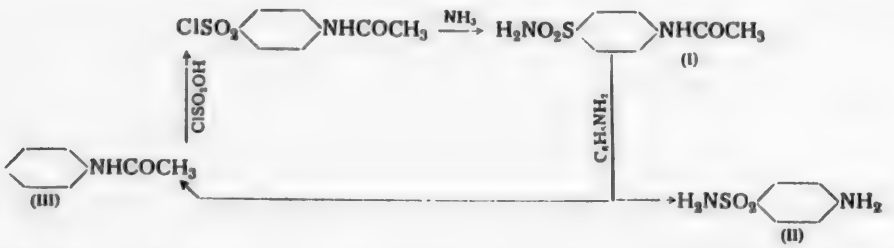
$$C_6H_5NH_2 \xrightarrow{(CH_3CO)_2O} C_6H_5NHCOCH_3 \xrightarrow{HOSO_2Cl} p\text{-}ClO_2SC_6H_4NHCOCH_3 \xrightarrow{NH_3}$$
$$\rightarrow p\text{-}H_2NO_2SC_6H_4NHCOCH_3 \xrightarrow{H_2SO_4} p\text{-}H_2NO_2SC_6H_4NH_2$$

is complicated and requires the consumption of a large number of starting products.

We developed a new method for the preparation of sulfanilamide, also based on the transamination reaction discovered by us

$$\underset{(I)}{p\text{-}H_2NO_2SC_6H_4NHCOCH_3} + C_6H_5NH_2 \rightleftharpoons \underset{(II)}{p\text{-}H_2NO_2SC_6H_4NH_2} + \underset{(III)}{C_6H_5NHCOCH_3}$$

The method proposed by us for the preparation of sulfanilamide, proceeding in three stages as a cyclic process by the scheme



is economical in that both the final product, sulfanilamide (II), and the starting product, acetanilide (III), are formed simultaneously at the stage of heating p-acetamidobenzenesulfonamide (I) with aniline, which leads to a reduction in the number of steps from 4 to 3 and a corresponding decrease in the consumption of aniline, acetic anhydride, sulfuric acid and other raw materials.

EXPERIMENTAL

Reaction of acetamide with the hydrochlorides of primary aromatic amines. Dry hydrogen chloride was passed into a solution of 1.5 g of acetamide in 20 ml of aniline for 15-20 minutes, and then the reaction mixture was heated in an oil bath at 180-190° for 45 minutes. The mixture after cooling was treated with 20 ml of 25% aqueous ammonia solution and then steam was passed into it. The solution after removal of the aniline by steam-distillation was cooled to give crystals with m. p. 114°. The mixed melting point with authentic acetanilide was not depressed. Yield 82%. In a similar manner the reaction of acetamide (1.5 g) with o-toluidine (30 ml) under the same conditions gave o-acetotoluidide; yield 46%. p-Acetamidodimethylaniline was obtained in 78% yield when 1.5 g of acetamide was heated with 4.37 g of p-aminodimethylaniline hydrochloride (180-190°, 45 minutes).

Reaction of acylarylamides with hydrochlorides of primary aromatic amines. A stream of dry hydrogen chloride was passed into a solution of 2 g of p-nitroacetanilide in 30 ml of aniline for 15-20 minutes, and then the reaction mixture was heated for 45 minutes in an oil bath at 180-190°. The mixture after cooling was treated with 20 ml of 25% aqueous ammonia solution and then steam-distilled. After removal of the aniline by steam-distillation the aqueous solution was cooled to give a crystalline substance with m. p. 147°, which did not depress the melting point when mixed with authentic p-nitroaniline. Evaporation of the mother liquor gave a crystalline substance, which did not depress the melting point when mixed with authentic acetanilide. The yield was nearly quantitative.

Under the same conditions the reaction of aniline (20 ml) with o-acetotoluidide (2 g) gave acetanilide and o-toluidine in quantitative yield. The reaction of aniline (25 ml) with 2.5 g of p-acetanisidide led to the formation of acetanilide and p-anisidine. In a similar manner, the reaction of aniline (25 ml) with p-acetamidobenzenesulfonamide (3 g), with p-acetamidodimetnylaniline (2 g), and with p-acetotoluidide (3 g), gave in all cases acetanilide and respectively p-aminobenzenesulfonamide, p-aminodimethylaniline (80% yield) and p-toluidine. The reaction under the same conditions of o-toluidine (30 ml) with p-nitroacetanilide (2 g), and also with acetanilide (3 g), led in both cases to the formation of o-acetotoluidide and respectively p-nitroaniline (quantitative yield) and aniline (75% yield).

SUMMARY

The following was established when the transamination of carboxylic acid amides was studied on a number of examples.

1. The reaction of acetamide with the hydrochlorides of aromatic amines yields the corresponding acylamide and ammonia.

2. The heating of the hydrochlorides of primary aromatic amines with acylarylamides yields a new acylarylamide and a new aromatic amine.

3. It is possible to utilize individual transamination reactions in the commercial production of certain amines. In the production of p-nitroaniline the authors recommend saponifying p-nitroacetanilide not with sulfuric acid, as is the practice at the present time, but instead with aniline, which leads to the simultaneous formation of both the final product p-nitroaniline and the starting product acetanilide, the latter being used in the same cyclic process to obtain p-nitroaniline. Similarly in the production of sulfanilamide the authors recommend saponifying the p-acetamidobenzenesulfonamide with aniline, which leads to the simultaneous formation of both sulfanilamide and starting acetanilide.

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MECHANISM OF THE REDUCTION OF γ-ACETOBUTYRONITRILE

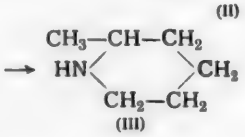
M. B. Braude

The reduction of γ-acetobutyronitrile (I) with sodium in butyl alcohol [1] yields two reaction products – 6-amino-2-hexanol (II, 17%) and 2-methylpiperidine (III, 15%).

S. M. Gurvich [2] postulated that the reduction proceeds according to scheme 1.

1. $CH_3COCH_2CH_2CH_2CN \xrightarrow{3H_2} CH_3\underset{\underset{OH}{|}}{CH}CH_2CH_2CH_2CH_2NH_2 \longrightarrow$

(I) (II)



(III)

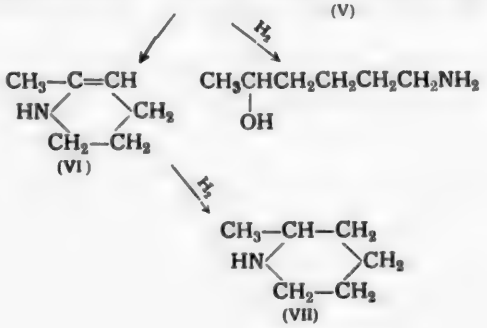
In order to increase the yield of needed 6-amino-2-hexanol we subjected γ-acetobutyronitrile to stepwise hydrogenation. The carbonyl group was reduced first, using the Meerwein-Pondorf method [3], and this gave δ-hydroxycapronitrile (IV, 84%).

$$CH_3COCH_2CH_2CH_2CN \xrightarrow{Al(OC_3H_7)_3} CH_3\underset{\underset{OH}{|}}{CH}CH_2CH_2CH_2CN \quad \text{(IV)}$$

The latter was then reduced with sodium in isoamyl alcohol to 6-amino-2-hexanol (47.7%). It should be mentioned that the formation of 2-methylpiperidine was not observed here.

Our data do not agree with the above reaction scheme proposed by Gurvich and we postulate that the intermediate product in the reduction of γ-acetobutyronitrile with sodium in alcohol is 6-amino-2-hexanone (V), i.e., the process goes according to scheme 2.

2. $CH_3COCH_2CH_2CH_2CN \xrightarrow{2H_2} [CH_3COCH_2CH_2CH_2CH_2NH_2]$ (V)



(VI) (VII)

To support our viewpoint we selectively reduced the CN group of γ-acetobutyronitrile in acetic anhydride using skeletal nickel catalyst. The 6-methyl-1,2,3,4-tetrahydropyridine (VI, 32% yield) obtained here was then reduced further with sodium in isoamyl alcohol to 2-methylpiperidine (VII, 74.5% yield). For identification purposes we prepared 6-methyl-1,2,3,4-tetrahydropyridine by the Gabriel method [4], which when reduced under similar conditions also gave 2-methylpiperidine. Gurvich considers the indicated reaction mechanism (scheme 2) to be impossible, citing the fact that tetrahydropyridines are not reduced by sodium in alcohol [2]. However, such applies only to the Δ^3-tetrahydropyridines [5], whereas the Δ^2-tetrahydropyridines are easily reduced to the corresponding piperidines [6].

Proceeding from the above, we believe that the reduction of γ-acetobutyronitrile proceeds through the intermediate stage of forming 6-amino-2-hexanone, which together with cyclization to 6-methyl-1,2,3,4-tetrahydropyridine, is simultaneously reduced to 6-amino-2-hexanol, i.e., the reaction goes according to the second scheme.

EXPERIMENTAL

γ-Acetobutyronitrile was obtained by the cyanoethylation of either acetone [1] or acetoacetic ester [7], and had the following constants:

B. p. 93-96° at 6 mm, 236-238° at 744 mm; $n^{20}D$ 1.4325, d^{20}_4 0.968, MR_D 29.68.

δ-Hydroxycapronitrile. To a boiling solution of 67 g of aluminum isopropylate in 150 ml of anhydrous isopropyl alcohol was added 17.5 g of γ-acetobutyronitrile. The reduction was run for 1 hour and 40 minutes. Then the reaction mass was worked up in the usual manner [3]. The obtained cyanohydrin was repeatedly extracted with ether, and the ether solution was washed with saturated magnesium sulfate solution and then dried. After removal of the ether by distillation the residue was vacuum-distilled. B. p. 106-108° at 4 mm, yield 15 g (84.2%). Light-yellow mobile liquid, readily soluble in water, and giving a negative test for the keto group.

$n^{20}D$ 1.4420, d^{20}_4 0.9641, MR_D 31.0; calculated 31.25.

Found %: N 12.37, 12.17. $C_6H_{11}ON$. Calculated %: N 12.39.

6-Amino-2-hexanol. Twenty-three grams of sodium metal was added in 40 minutes to a boiling solution of 17 g of δ-hydroxycapronitrile in 450 ml of isoamyl alcohol. The mixture was heated until all of the sodium had dissolved. After cooling, the mixture was treated with water and then with concentrated hydrochloric acid until acid to Congo. The isoamyl alcohol and water were removed in vacuo, and the residue, a thick slurry, was heated with alcohol. The alcohol solution was filtered from insoluble salts, and then evaporated in vacuo to dryness. The residue was treated with 40% sodium hydroxide, and the separated base was extracted with chloroform. The chloroform solution was dried over potash. After removal of the chloroform by distillation we obtained 8.5 g (47.7%) of 6-amino-2-hexanol with b. p. 96-97° at 5 mm. The substance is a strongly alkaline colorless liquid, readily soluble in water, alcohol and chloroform, and difficultly soluble in ether.

$n^{20}D$ 1.4605, d^{20}_4 0.9210, MR_D 34.76; calculated 34.98.

Found %: N 12.13, 12.20. $C_6H_{15}ON$. Calculated %: N 11.96.

Reaction of 6-amino-2-hexanol with thionyl bromide at 4-8° gave 2-bromo-6-aminohexane hydrobromide. The latter had m. p. 95-102° (in a sealed capillary), is readily soluble in water, alcohol and acetone, and is insoluble in ether and benzene.

Found %: N 5.18; 5.26. $C_6H_{15}NBr_2$. Calculated %: N 5.36.

6-Methyl-1,2,3,4-tetrahydropyridine. A solution of 5 g of γ-acetobutyronitrile in 20 ml of acetic anhydride was hydrogenated for 4 hours in the presence of skeletal nickel catalyst (3.5 g) at room temperature and a pressure of 1.5 atm. After removal of the catalyst the excess acetic anhydride was vacuum-distilled. The residue was boiled with 20% hydrochloric acid for 4 hours, after which the solution was evaporated to dryness. The obtained crystalline precipitate was treated with boiling anhydrous alcohol, the alcohol solution was concentrated, the residue was treated with 40% sodium hydroxide solution, and the separated base was extracted with ether. After removal of the ether by distillation we collected the fraction with b. p. 130-132° at 747 mm, $n^{20}D$ 1.4560. Yield 1.4 g (32.1%).

The colorless liquid is soluble in water, alcohol and ether. It darkens on standing. Picrate (from alcohol), m. p. 120.5-121°. The mixed melting point with the picrate of the 6-methyl-1,2,3,4-tetrahydropyridine obtained by the Gabriel method [4] was not depressed. The mixed melting point with the picrate of 2-methylpiperidine was depressed.

2-Methylpiperidine. Sodium metal (7 g) was added to a boiling solution of 2.9 g of 6-methyl-1,2,3,4-tetrahydropyridine in 100 ml of isoamyl alcohol. As a reaction result we obtained 2.2 g (74.5%) of 2-methylpiperidine with b. p. 115-117° and $n^{20}D$ 1.4475. The picrate after recrystallization from water had m. p. 132-132.5°, and the hydrochloride had m. p. 209.5-210.5°. The mixed melting point with authentic 2-methylpiperidine hydrochloride was not depressed.

SUMMARY

1. It was found that the stepwise reduction of γ-acetobutyronitrile increases the yield of 6-amino-2-hexanol from 17 to 40%.

2. It was shown that the reduction of γ-acetobutyronitrile with sodium in alcohol proceeds through the intermediate stage of forming 6-amino-2-hexanone, which together with cyclization to 6-methyl-1,2,3,4-tetrahydropyridine, with subsequent reduction to 2-methylpiperidine, is simultaneously reduced to 6-amino-2-hexanol.

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** In Russian.

RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

IX. SYNTHESIS OF BISAZO DYES BY THE CONDENSATION OF DIAZO COMPOUNDS WITH SALTS OF N-ARYL QUINALDINES

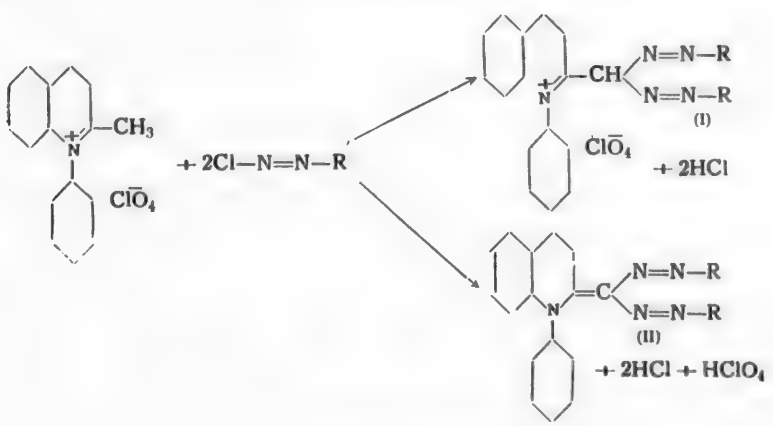
G. T. Piliugin and S. V. Shinkorenko

Among the numerous reactions of diazonium salts there are only a few investigations connected with the coupling of diazo compounds with heterocyclic methylene bases and with quaternary salts of heterocylic compounds. Coupling has been observed at an active methyl group with onium compounds of quinaldine and lepidine [1-4], with various heterocyclic bases and their salts [5, 6] and with monohydroxydihydropyrimidines [7]. The reactions have been investigated of diazonium salts with methylbenzimidole [8], with active methyl groups on heterocyclic compounds [9], with methylbenzthiazole [10] and with quaternary salts of heterocyclic nitrogen compounds containing active methyl groups in the α- and γ- positions relative to the nitrogen [11].

While studying the chemical transformations of quaternary salts of derivatives of quinoline containing aromatic radicals on the hetero nitrogen atom, which we had prepared [12], interest arose in the coupling of these salts with diazonium compounds. Investigations of this type are not found in the literature. These salts, containing as they do electrophilic radicals, should couple relatively easily with diazohydrates, diazotates and diazonium salts with the formation of ionic dyes.

This communication is concerned with the coupling of N-phenylquinaldine perchlorate with phenyldiazonium chloride and with p-nitrophenyldiazonium chloride.

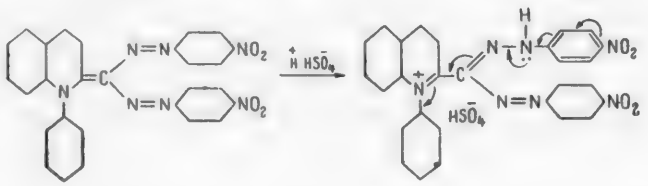
The azo coupling reaction could proceed according to the following schemes:



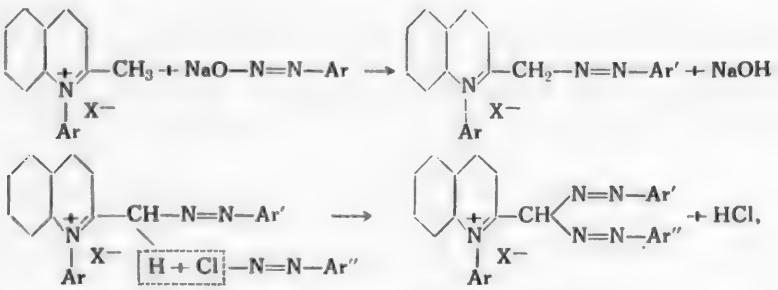
R = C_6H_5 & p-$O_2NC_6H_4$.

Investigation of the dyestuffs isolated showed that under our reaction conditions bis-(phenylazo)-N-phenyl-2-quinolinemethane perchlorate (I) with an absorption maximum at 458 mμ and bis-(p-nitrophenylazo)-N-phenyl-2-quinolinemethane (II) with an absorption maximum at 588 mμ, were formed. It is very strange that on coupling

with the p-nitrophenyldiazonium salt a dye that does not contain an anion was formed whereas on coupling with the phenyldiazonium salt a salt-type dye was isolated. It must be assumed that the effect of the nitro group in the diazonium salt markedly weakens the basic character of the hetero nitrogen atom such that it is unable to form salts. It was noted that on addition of concentrated sulfuric acid to crystals of the dye a beautiful, intense blue coloration was formed. This phenomenon is connected with salt formation by an increase in the electrophilic character of the hetero nitrogen atom and by the redistribution of the electron density of the molecule as a whole, which is also the cause of the deepening in color.



It is interesting to note that similar bisazo dyes can be synthesized also by a stepwise method in two stages, which is of considerable value for the synthesis of bisazo dyes of an unsymmetrical structure.



where X-anion; Ar, Ar', Ar''-aromatic radical

The preparation of bisazo dyes is also not devoid of practical interest. Thus on coupling (depending on the conditions) the dye remains in a soluble form and only on neutralizing with ammonia or sodium carbonate does it manifest itself in coming down as a precipitate. Experiments have shown that on impregnation of cotton or fabrics with the soluble components and subsequently treating with ammonia vapor or sodium carbonate solution the dye becomes fixed on the cotton. Moreover the separated dyes possess indicator properties, particularly those containing nitro groups in the molecule. There might also be some interest in the fact that these coloring materials form colored complexes with metals. These preliminary indications could be brought into practical use by suitable investigation.

EXPERIMENTAL

Coupling of N-phenylquinaldine perchlorate with phenyldiazonium chloride. To a solution of 5.0 g of N-phenylquinaldine perchlorate in 50 ml of quinoline, cooled to 0°, a solution of phenyldiazonium chloride prepared from 3 ml of aniline was added, whereupon an intense red-orange coloration appeared immediately. No dye had precipitated after 10 hours; the reaction mixture was treated a few times with ether, as a result of which the dye came down in the form of an orange powder. The product was boiled with water for the removal of salts. 7.0 g of dye of a brick-red color was obtained (84.3%). Dye formation also occurred if glacial acetic acid or aqueous pyridine was used in place of quinoline. After recrystallizing the dye from alcohol and then from aqueous acetone it melted at 234° (decomp.) and consisted of a fine crystalline material of a brick-red color with a yellow luster. The dye dissolved readily in acetone, pyridine, quinoline and chloroform, and was practically insoluble in ether, benzene and toluene. The absorption maximum of the dye in ethanol was at 458 mμ. The absorption curve was plotted by a recording spectrophotometer SF-2M.

Found %: Cl 6.45, 6.37; N 13.40. $C_{28}H_{22}O_4N_5Cl$. Calculated %: Cl 6.71; N 13.26.

Coupling of N-phenylquinaldine perchlorate with p-nitrophenyl-diazonium chloride. To a solution of 5.0 g of phenylquinaldine perchlorate in 70 ml of glacial acetic acid a solution of p-nitrophenyldiazonium chloride, prepared from 4.3 g of p-nitroaniline, was added with cooling. After mixing the solutions no color change was observed even after some hours. On neutralizing with sodium carbonate a dye began to separate immediately in the form of a dark blue powder. The yield of crude product was 8.0 g (92.6%). For purification the substance was boiled with water a few times, reprecipitated from pyridine and recrystallized from alcohol-water. The dye, consisting of fine crystals of a dark blue color, with m. p. 209-210°, dissolved readily in pyridine, chloroform, acetone, acetic acid and dioxan; it was practically insoluble in ether, benzene and toluene. In concentrated sulfuric acid the dye dissolved with a pure blue color. The acetic acid solution was a red-orange color becoming blue with alkalis. It should be noted that this dye changes color depending on the solvent. Thus in pyridine, dioxan and chloroform it acquires a blue color, in alcohol and acetone – a violet, and in acetic acid and ethyl acetate a red-orange color. A similar phenomenon, called solvatochromism, is met with in many internally ionized coloring materials, the depth of color is connected with the nature of the dye and with the degree of polarization [13]. The absorption maximum of the dye in ethanol is at 588 mμ.

Found %: N 18.62, 18.63. $C_{28}H_{19}O_4N_7$. Calculated %: N 18.94.

SUMMARY

1. The possibility has been shown of the interaction of salts of N-arylquinaldines at the α-methyl group with diazonium salts, with the formation of a new type of bisazo dye (two azo groups on one carbon atom).

2. The interaction of N-phenylquinaldine perchlorate with phenyldiazonium chloride and with p-nitrophenyldiazonium chloride has been studied. As a result two azo dyes have been isolated and characterized – bis(phenylazo)-N-phenyl-2-quinolinemethane perchlorate, with an absorption maximum at 458 mμ, and bis-(p-nitrophenyl-azo)-N-phenyl-2-quinolinemethane, with an absorption maximum at 588 mμ.

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RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

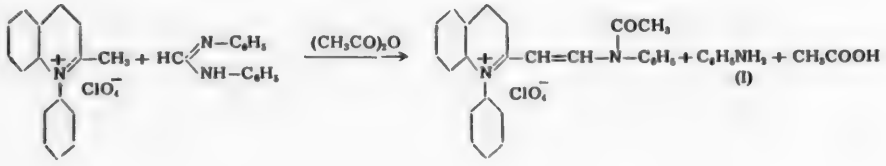
X. SYNTHESIS OF N-ARYL-2-β-ANILINOVINYLQUINOLINE DERIVATIVES AND THEIR TRANSFORMATIONS

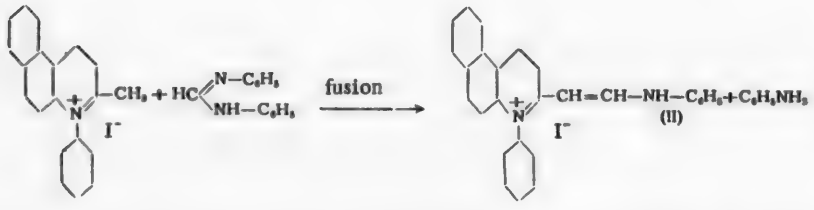
G. T. Pilugin, E. P. Opanasenko and S. V. Shinkorenko

For the synthesis of trimethinecyanine dyes of unsymmetrical structure substances prepared from diphenylformamidine and quaternary salts of heterocyclic bases are most often used [1, 2]. These intermediate products are prepared mainly from haloalkylates of methylbenzthiazole and trimethylindolenine, and much more rarely from other heterocyclic compounds. On condensing the above-mentioned substances with other quaternary salts unsymmetrical trimethinecyanines are obtained [3-7].

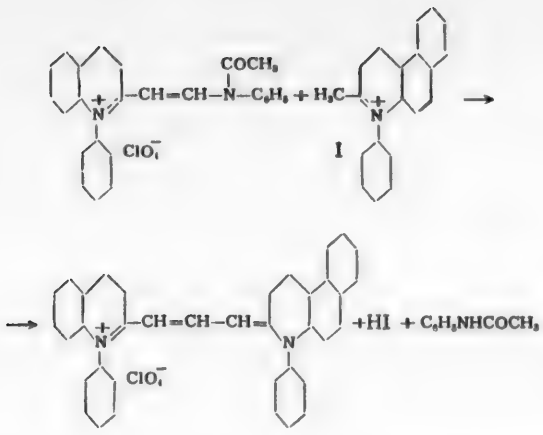
With the object of expanding the field of organic synthesis and of carrying out a more detailed investigation of the properties of the unsymmetrical molecules we undertook the synthesis of analogous intermediate products from quinoline derivatives containing aryl radicals on the hetero-nitrogen atom.

In this communication results of condensation of diphenylformamidine with N-phenylquinaldine perchlorate and N-phenylbenzoquinaldine iodide which proceeded as in the following scheme, are presented.





The substances obtained, N-phenyl-2-β-acetanilinovinylquinoline perchlorate (I) and N-phenyl-2-β-anilinovinyl-5,5-benzoquinoline iodide (II) were condensed with quaternary salts of quinaldine and benzthiazole derivatives with the formation of unsymmetrical trimethinecyanines.



It is known that unsymmetrical trimethinecyanine dyes differ markedly in properties from the corresponding symmetrical dyes. The asymmetry of the molecules brings about, in particular, a reduction in the strength of the electronic vibrations, as a direct consequence of which there is a marked reduction in the intensity of the molecular absorption of the unsymmetrical dyes in all cases without exception. It is of no less interest that the asymmetry of the molecules also has a strong effect on the superposition of the complex electronic movements, with the result that in the case of the unsymmetrical molecules, made up of heterocyclic bases differing in nature, the secondary shortwave absorption maxima are absent. On the other hand these maxima are always strongly expressed in the case of symmetrical quinoline and indolenine carbocyanine molecules.

The unsymmetrical dyes prepared by us, with quinoline perichromes at the ends of the polymethine chains have absorption maxima that show very little shift towards the shortwave part of the spectrum. This indicates that the nature of the secondary maxima is connected with the interaction of the electrons of the heterocyclic nucleus with the electron cloud of the main polymethine chromophore.

The carbocyanines synthesized from the intermediate products obtained are indicated in the Table.

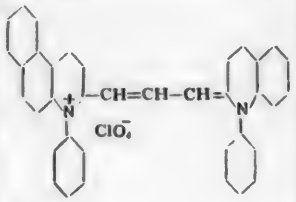
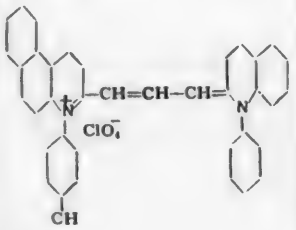
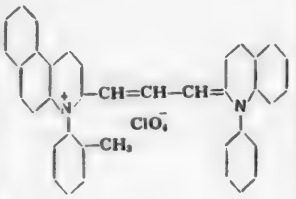
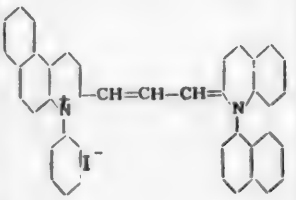
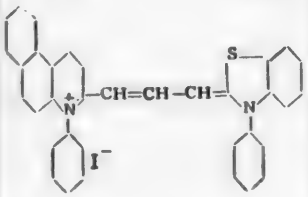
EXPERIMENTAL

N-Phenyl-2-β-acetanilinovinylquinoline perchlorate. 0.5 g of 1-phenylquinaldine perchlorate, 0.4 g of diphenylformamidine and 3 ml of acetic anhydride were heated for 20 minutes at the boiling point of the reaction mixture, during which time the mixture acquired a bright green color. The intermediate product, phenylacetanilinovinylquinoline perchlorate, crystallized out from the reaction mixture in the form of dark green crystals which were filtered off and washed on the filter with alcohol. In cases where the product did not crystallize out the reaction mixture was treated with ether until the ether no longer became colored. The reaction product which comes out as a resin, was boiled with water for removal of the quaternary salt and rubbed with a rod in the presence of alcohol until it became converted to a solid, powdery condition. After recrystallizing from acetic acid 0.24g(33%) of product was obtained. This material dissolves in acetone, on heating in alcohol and acetic acid, and is not soluble in ether, benzene, toluene, chloroform. After twice recrystallizing from glacial acetic acid the intermediate product consisted of light green crystals of m. p. 255° (decomp.).

Found %: Cl 7.60; N 5.67, 6.11. $C_{25}H_{21}O_4N_2Cl$. Calculated %: Cl 7.62; N 6.02.

N-Phenyl-2-β-anilinovinyl-5,6-benzoquinoline iodide. A mixture of 0.5 g of 1-phenyl-5,6-benzoquinaldine iodide and 0.5 g of diphenylformamidine was ground vigorously in a mortar and melted on a water bath at 90° for 1 hour. The dark melt was treated with boiling water then with alcohol. By this means the quaternary salt, diphenylformamidine and possibly any symmetrical dye formed were dissolved in the alcohol and the intermediate product came out in the form of crystals, which after recrystallizing from a large quantity of alcohol melted at 300-301°. Yield 0.23 g (37.5%).

Found %: I 25.25, 25.08. $C_{27}H_{21}N_2I$. Calculated %: I 25.36.

No.	Formula of dye (I) (II)	Absorption maximum (in mμ) •				Shift from additivity		M.p.
		symm. from (I)	symm. from (II)	symm. from $\frac{(I)+(II)}{2}$	unsymm. found	hypsochromic	bathochromic	
1		645 595	614 566	629.5	624 582	5.5	—	257° (decomp.)
2		642 592	614 566	628.0	625 580	3.0	—	251 (decomp.)
3		644 600	614 566	629	623 578	6.0	—	276 (decomp.)
4		645 595	618 574	631.5	625 580	6.5	—	279 (decomp.)
5		645 595	558	601.5	596	5.5	—	220 (decomp.)

The intermediate products prepared and characterized, were condensed with salts of N-phenylquinaldine, N-phenylbenzoquinaldine, N-(p-tolyl)-benzoquinaldine, N-(α-naphthyl)-quinaldine and N-ethylbenzthiazole in a medium of pyridine with the addition of a small quantity of acetic anhydride. As a result of this the unsymmetrical carbocyanines were isolated.

• In the absorption maxima the first number is the main maximum and the second number is the secondary shortwave maximum.

(1-Phenyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was obtained by condensation of 1-phenylacetanilinovinylquinoline perchlorate with 1-phenyl-benzoquinaldine iodide. The recrystallized, unsymmetrical carbocyanine melted at 257° (decomp.). The absorption maxima of the dye were at 624 and 582 mμ in ethanol.

Found %: Cl 5.85, 5.80. $C_{37}H_{27}O_4N_2Cl$. Calculated %: Cl 5.91.

(1-p-Tolyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was synthesized from 1-phenylacetanilinoquinoline perchlorate and 1-p-tolylbenzoquinaldine iodide. M. p. 251° (decomp.). The absorption maxima were at 625 and 580 mμ.

Found %: Cl 5.54, 5.63. $C_{38}H_{27}O_4N_2Cl$. Calculated %: Cl 5.78.

(1-o-Tolyl-5,6-benzoquinoline-2)-(1-phenylquinoline-2)-trimethinecyanine perchlorate was synthesized from 1-phenylacetanilinovinylquinoline perchlorate and 1-o-tolylbenzoquinaldine iodide. The dye melted at 276° (decomp.). The absorption maxima were at 623 and 578 mμ.

Found %: Cl 5.63, 5.59. $C_{38}H_{27}O_4N_2Cl$. Calculated %: Cl 5.78.

(1-α-Naphthylquinoline-2)-(1-phenyl-5,6-benzoquinoline-2)-trimethinecyanine iodide was prepared by condensation of 1-phenylanilinovinylbenzoquinoline iodide with 1-α-naphthylquinaldine iodide. M. p. 279° (decomp.). The absorption maxima in ethanol were at 625 and 580 mμ.

Found %: I 18.52, 18.63. $C_{41}H_{29}N_2I$. Calculated %: I 18.76.

(1-Phenyl-5,6-benzoquinoline-2)-(3-ethylbenzthiazole-2) trimethinecyanine iodide was prepared by heating 1-phenylanilinovinylbenzoquinoline iodide with 2-methylbenzthiazole ethyliodide and also, as a control, from 2-β-acetanilinovinylbenzthiazole ethyliodide and 1-phenyl-5,6-benzoquinaldine iodide. Exactly the same dye was obtained in both cases. M. p. 220° (decomp.). The absorption maximum was at 596 mμ.

Found %: I 21.32, 21.46. $C_{31}H_{25}N_2I$. Calculated %: I 21.69.

SUMMARY

1. The following new compounds, which are not described in the literature, have been synthesized: N-phenyl-2-β-acetanilinovinylquinoline perchlorate and N-phenyl-2-β-anilinovinyl-5,6-benzoquinoline iodide.

2. By condensation of the above-mentioned compounds with quaternary salts of heterocyclic bases 5 new, unsymmetrical carbocyanines have been prepared: a) (N-phenyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; b) N-(p-tolyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; c) N-(o-tolyl-5,6-benzoquinoline-2)-(N-phenylquinoline-2)-trimethinecyanine perchlorate; d) (N-phenyl-5,6-benzoquinoline-2)-(N-α-naphthylquinoline-2)-trimethinecyanine iodide; e) (N-phenyl-5,6-benzoquinoline-2)-(3-ethylbenzthiazole-2)-trimethinecyanine iodide.

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RESEARCH IN THE FIELD OF SYNTHETIC DYESTUFFS

XL. CONDENSATION OF SALTS OF N-ARYLQUINALDINE WITH NITROSO COMPOUNDS

G. T. Piliugin and S. V. Shinkorenko

By the interaction of primary aromatic amines and aldehydes, Schiff's bases or azomethine compounds are formed [1].

$$ArNH_2 + OCHAr' \rightleftarrows ArN{=}CHAr' + H_2O$$

It has been shown that azomethine compounds are also formed by condensing aromatic nitrosamines or nitrosophenols with compounds containing methylene or methyl groups with labile hydrogen atoms [2-4].

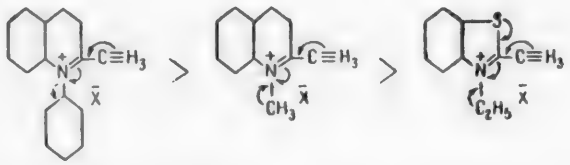
For this reaction sufficient lability of the hydrogen atom is ensured by the presence of such electrophilic groups as CN, NO_2, COOH, CHO etc., which by displacing the electron cloud weaken the bond between the hydrogen and carbon atoms [5].

In view of the relative lability of the hydrogen atoms of a methyl group in the α-position of quinaldine, 6-methylquinaldine and mesomethylacridine the reaction of these with nitroso compounds has been studied [6]; it was shown that in the form of the free base only mesomethylacridine took part in this reaction with the formation of an azomethine, while quinaldine and lepidine did not react.

Haloalkylates of quinaldine, lepidine and picoline, being more reactive, react readily with nitroso compounds with the formation of azomethine compounds [7]. The azomethine compounds prepared by condensation of quaternary salts of benzthiazole and indolenine with nitroso compounds have been studied [8]. It was shown that the azomethines are more deeply colored than the corresponding styryl derivatives.

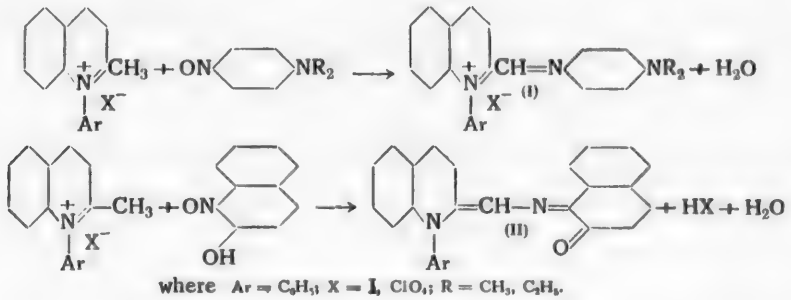
The azomethine compounds are of definite scientific interest because they are deeply colored and on heating with dilute acids can be split with the formation of aldehydes and primary amines. Furthermore the azomethine dyes are used in color photography by use of multilayer films with color development of the image in depth, in the form of dyes [9].

Thus bearing in mind the considerable importance of the azomethine compounds it was of interest to study the reaction of some new N-arylquinaldine quaternary salts, prepared by us, with aromatic nitroso compounds. In consequence of the presence in these onium compounds of electrophilic radicals on the hetero nitrogen atom the hydrogen atoms of the methyl group in the α-position are more labile than in the haloalkylates of quinaldine and 2-methylbenzthiazole [10].



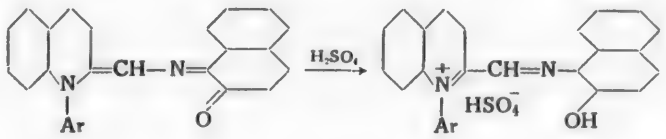
It was assumed that the reaction in question should take place relatively easily. As a result of this reaction

it is possible to form azomethine coloring materials that have not previously been described in the literature. We carried out the condensation of N-phenylquinaldine perchlorate and N-phenyl-5,6-benzoquinaldine iodide with p-nitrosodimethylaniline and p-nitrosodiethylaniline, and also with α-nitroso-β-naphthol. The reaction proceeded according to the scheme:



where Ar = C_6H_5; X = I, ClO_4; R = CH_3, C_2H_5.

The absorption maxima of these salt-type azomethines are in a longer wavelength part of the spectrum than those of the corresponding styryl derivatives and in a shorter wavelength part in comparison with the carbocyanines. By condensation of the salts with nitroso-β-naphthol, hydroxyazomethine dye bases were obtained, this being confirmed by analysis and by the identity of the absorption spectrum curves in neutral and alkaline solution. On converting the dyes to the salt form by the addition of sulfuric or hydrochloric acids the color is increased in consequence of the lowering of the energetic level of the molecule and the change in structure.



Hydroxyazomethines change color depending on the solvent, i.e., they possess the property of solvatochromism. The condensation of nitroso compounds with N-arylquinaldine salts goes very smoothly without the use of condensing agents, which indicates the high reactivity of the methyl group.

EXPERIMENTAL

4-Dimethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate. A mixture of 1.5 g of N-phenylquinaldine perchlorate, 0.7 g of p-nitrosodimethylaniline and 30 ml alcohol was heated on the water bath in a flask fitted with a reflux condenser. About 1.5 hours after the reaction mixture reached boiling point a crystalline precipitate began to separate in the form of small needles with a green luster. Further heating was accompanied by bumping, hence heating was discontinued after 15 minutes. On the following day the dye precipitated was filtered off and washed with alcohol. The filtrate was again heated up to the point of separation of dye. In all 1.45 g (68.4%) of dye was obtained. The dye was recrystallized from alcohol and then from aqueous alcohol (1:1). The melting point of the substance was 251-252°. Absorption maximum in ethanol, 587 mμ. The absorption curve was plotted on a recording spectrophotometer SF-2M.

Found %: Cl 8.04, 7.78. $C_{24}H_{22}O_4N_3Cl$. Calculated %: Cl 7.84.

4-Diethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate. 1.5 g of N-phenylquinaldine perchlorate, 0.84 g of p-nitrosodiethylaniline and 30 ml of alcohol were placed in a flask fitted with a reflux condenser and heated on a boiling water bath for 1 hour 40 minutes. On the following day the dye was filtered off and washed with alcohol, and the filtrate was heated again for 20 minutes; an additional quantity of material was thus obtained. Yield 1.4 g (62.2%). The dye was crystallized from alcohol and then from aqueous alcohol (2:3). Long needles with a green luster. M. p. 252°. Absorption maximum, 587 mμ.

Found %: Cl 7.67, 7.42. $C_{26}H_{26}O_4N_3Cl$. Calculated %: Cl 7.38.

4-Dimethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide. 0.57 g of p-nitrosodimethylaniline, 1.5 g of N-phenyl-5,6-benzoquinaldine iodide and 40 ml of alcohol were placed in a flask fitted with a reflux condenser and heated on a boiling water bath for 30 minutes, after which the dye began to separate in the form of small needles with a bronze luster. After about 10 hours the precipitated dye was filtered and the filtrate was again heated on the water bath for 20 minutes, after which more dye precipitated. 1.02 g (51.2%) of the dye was obtained. After recrystallizing the dye from aqueous alcohol (1:1) it consisted of long, green lustrous needles with m. p. 273°. Absorption maximum in ethanol, 573 mμ.

Found %: I 23.90, 23.67. $C_{28}H_{24}N_2I$. Calculated %: I 23.97.

4-Diethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide. A mixture of 1.5 g of N-phenyl-5,6-benzoquinaldine iodide, 0.65 g of p-nitrosodiethylaniline and 30 ml of alcohol were heated on a boiling water bath in a flask fitted with a reflux condenser. After 30 minutes from the time that the reaction mixture reached boiling point a crystalline precipitate began to separate, whereupon heating was discontinued because of bumping. The crystals were filtered off and the filtrate was reheated until crystals again began to separate. Yield of dye 0.95 g (45.2%). After recrystallizing from aqueous alcohol (3:2) the dye was obtained as small needles with a green luster and m. p. 276°. Absorption maximum in ethanol, 574 mμ.

Found %: I 22.79, 22.88. $C_{30}H_{28}N_2I$. Calculated %: I 22.76.

2-Oxonaphthyl-1-(1'-phenylquinoline-2)-azomethine. The directions of Kiprianov and Fridman [8] were taken as the basis of the synthesis of this compound. A mixture of 0.5 g of N-phenylquinaldine perchlorate and 0.25 g of α-nitroso-β-naphthol was dissolved by heating in 5 ml alcohol. To the hot alcoholic solution were added 2-3 drops of piperidine whereupon the color of the reaction mixture changed immediately from yellow-brown to blue-green. On standing, a resinous substance separated from the reaction mixture, which on addition of 5 ml of water and trituration was converted to a crystalline powder with a bronze cast. Yield 0.54 g (91.5%). After recrystallizing the dye from alcohol small leaf-type crystals with a bronze cast and m. p. 167-168° were obtained. Absorption maximum in ethanol, 660 mμ. A test for halide was negative. The absorption maximum in neutral and alkaline solution was unchanged. The azomethine dye obtained had the structure of the free base (II).

2-Oxonaphthyl-1-(1'-phenyl-5,6-benzoquinoline-2'-)-azomethine. 0.5 g of N-phenyl-5,6-benzoquinaldine iodide and 0.22 g of α-nitroso-β-naphthol were dissolved on heating in 5 ml alcohol; 2-3 drops of piperidine were added whereupon the color of the solution changed immediately, becoming blue-green. 5 ml of water was added to the reaction mixture and on standing the dye separated in the form of a dark blue crystalline powder with a bronze cast. The dye was recrystallized from an acetone-water mixture (10:1); long needles with a bronze luster and m. p. 198-200°. Yield of product, 0.44 g (83%). Absorption maximum in ethanol, 659 mμ. The analytical data indicate that this azomethine dye does not have a salt-type structure.

Found %: N 6.55, 6.51. $C_{30}H_{20}ON_2$. Calculated %: N 6.59.

SUMMARY

1. By condensing salts of N-arylquinaldines, containing an active methyl group in the α-position, with nitrosamines, four azomethine dyes not described in the literature, have been obtained: a) 4-dimethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate; b) 4-diethylaminophenyl-1-(1'-phenylquinoline-2'-azomethine) perchlorate; c) 4-dimethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide; and d) 4-diethylaminophenyl-1-(1'-phenyl-5,6-benzoquinoline-2'-azomethine) iodide.

2. Two azomethine dye bases have been prepared by condensing salts of N-arylquinaldines with α-nitroso-β-naphthol: a) 2-oxonaphthyl-1-(1'-phenylquinoline-2)-azomethine and b) 2-oxonaphthyl-1-(1'-phenyl-5,6-benzoquinoline-2')-azomethine.

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THE REDUCTION OF THE BISULFITE COMPOUND OF 1-NAPHTHOL

I. 1,2-DIHYDRONAPHTHALENE-2-SULFONIC ACID

S. V. Bogdanov

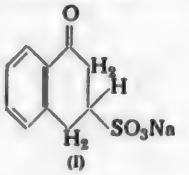
It has been reported [1] that the bisulfite compound of 1-naphthol behaves as a ketone with respect to hydroxylamine and semicarbazide, being converted to the oxime and semicarbazone of the bisulfite compound. On these grounds the structure 1-oxo-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (I) has been proposed for this compound.

According to the literature [2,3] reduction of 1-oxo-1,2,3,4-tetrahydronaphthalene leads to 1-hydroxy-1,2,3,4-tetrahydronaphthalene and 1,1'-dihydroxy-1,1'-ditetralin. It seemed of interest to follow the reduction of the bisulfite compound of 1-naphthol also.

Experiment showed that by the action of zinc and dilute acetic acid in the presence of copper sulfate the bisulfite compound of 1-naphthol is converted to a mixture of reduction products from which the sodium salt of 1,2-dihydronaphthalene-2-sulfonic acid (II) was isolated. The formation of the dihydronaphthalenesulfonic acid (II) can be explained by dehydrogenation of 1-hydroxy-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid formed as an intermediate product. Using the pure bisulfite compound under the above conditions the yield of the sulfonic acid (II) was 52-55% and the residual bisulfite compound was 6%. With impure bisulfite compound containing mineral salts and a small amount of 1-naphthol sulfonic acids as impurities the reaction did not proceed so well.

The sodium salt of dihydronaphthalenesulfonic acid is stable under normal conditions but on heating with dilute caustic alkalis and with mineral acids it behaves as a bisulfite compound of naphthalene and breaks down into naphthalene and sulfurous acid; under reducing conditions the naphthol bisulfite compound is unchanged. In contrast to the naphthol bisulfite compound it reacts with bromine in an aqueous medium and is stable under the conditions for the iodometric analysis of a bisulfite compound [4]. The content of the sulfonic acid (II) in the solution of the bisulfite compound reduction products was determined by the bromide-bromate method (1 molecule of sulfonic acid requires 2 atoms of bromine), and the residual bisulfite compound by its decomposition with alkali and titration of the sulfurous acid with iodine. The other bisulfite compound reduction products showed no noticeable effect on the analytical results under the conditions chosen.

The sulfonic acid (II) with bromine-water adds on a molecule of hypobromous acid and is converted to 4-hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (III). This addition of hypobromous acid to (II) corresponds to the conversion of 1,2-dihydronaphthalene to 1-hydroxy-2-chloro-1,2,3,4-tetrahydronaphthalene by the action of hypochlorous acid [2].



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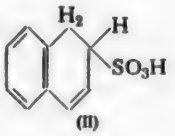
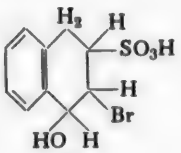


(II)



(III)

The bromine derivative (III) forms a mixture of naphthalene and 2-bromonaphthalene with 40% sulfuric acid and, with 10% sodium hydroxide, converts it to naphthalene-2-sulfonic acid. These transformations indicate the structures of the bromine derivative (III) and the dihydronaphthalenesulfonic acid (II), and hence they confirm structure (I) for the bisulfite compound of 1-naphthol.

EXPERIMENTAL

The bisulfite compound of 1-naphthol (I) used in the reduction experiments was prepared from 1-naphthol and was recrystallized from aqueous alcohol. The presence of 1-naphthol sulfonic acids in the impure bisulfite compound was shown by converting them to the corresponding nitroso compounds. The aqueous solution of the residue obtained by evaporating down the filtrate from recrystallization of the bisulfite compound was treated with alkali, acidified and the 1-naphthol extracted with ether. On addition of nitrite to the aqueous part 4-nitroso-1-naphthol-2-sulfonic acid precipitated, and was characterized by the absence of a coloration with ferrous sulfate and by conversion on heating with nitric acid to 2,4-dinitronaphthol with m. p. 138-139° (decomp.). The filtrate from this nitroso compound gave a green coloration with ferrous sulfate indicating the presence of 2-nitroso-1-naphthol-4-sulfonic acid. 1-Naphthol-4-sulfonic acid was also found in the filtrate from the salted-out bisulfite compound. After removal of residual bisulfite compound it was converted to 2-nitroso-1-naphthol-4-sulfonic acid which gave an intense green coloration with ferrous sulfate, was converted to 2,4-dinitro-1-naphthol by the action of nitric acid and on reduction gave 2-amino-1-naphthol-4-sulfonic acid. The latter was characterized by conversion to 2-diazo-1-naphthol-4-sulfonic acid and to 1,2-naphthoquinone-4-sulfonic acid. Sulfonation of the naphthol during the preparation of the bisulfite compound probably arises from the simultaneous action of sulfurous acid and air [5].

1,2-Dihydronaphthalene-2-sulfonic acid (II). To a solution of 21.1 g of 94.19% bisulfite compound (I) and 2 g of copper sulfate in 200 ml of water at 50°, acidified with 40 ml of 98% acetic acid, 21 g of zinc dust was added over a period of half an hour and the mixture was stirred for 4 hours at 90-92°. The unreacted zinc (10.7 g) was filtered off and the filtrate was made up to 500 ml with water. For determination of the yield of the sulfonic acid (II), to 25 ml of the solution was added 175 ml of water, 10 ml of hydrochloric acid and 10 ml of a 20% potassium bromide solution, and the mixture was titrated with 0.2N potassium bromate to reaction with starch-iodine paper. At this point the previously colorless solution acquires a faint yellow color. For determination of residual bisulfite compound another 25 ml of the solution was made alkaline with 25 ml of 37% sodium hydroxide; after 15 minutes it was diluted with 1.5 liters of water, acidified with 40 ml of hydrochloric acid and titrated with 0.1N iodine. The yield of sodium salt of the sulfonic acid (II) was 10.22 g (55%) and the residual bisulfite compound was 1.26 g (6.3%). To the remaining solution, after evaporating down to 180 ml, 36 g sodium chloride was added and the sodium salt of the sulfonic acid (II) that separated was filtered off and washed with alcohol. Yield 8.9 g (78.6%).

In 18 similar experiments the yield of the sulfonic acid (II) in solution was 52-55%. From all the solutions, corresponding to 1.36 moles bisulfite compound, 163.5 g (39.6%) of 76.5% sodium salt of sulfonic acid (II) was isolated.

On reduction of the bisulfite compound in the absence of copper sulfate, solution of the zinc was strongly retarded and the yield of the sulfonic acid (II) was poor. The use of impure bisulfite compound resulted in rapid and almost complete solution of the zinc, a fall in the yield of the sulfonic acid (II) to 20-30% and an increase in the unreacted bisulfite compound.

In order to test the stability of the sulfonic acid (II) under reducing conditions 4.92 g of 94.4% sodium salt (II) was treated as above with zinc and acetic acid in the presence of copper sulfate for 7.5 hours. In the filtrate after removal of residual zinc 98.5% of the original material was found by bromate titration. From the main part of the filtrate after concentrating and salting out, 4.12 g, corresponding to 0.018 mole of sulfonic acid taken, of 94.04% sodium salt was isolated. Yield 92.7%.

The sodium salt of dihydronaphthalenesulfonic acid (II) crystallizes in colorless, thick, tetragonal plates (from aqueous alcohol or water), dissolving readily in water and with difficulty in alcohol; it contains no water of crystallization.

Found %: C 51.42, 51.50; H 4.13, 4.10; Na 9.71, 9.86. M (bromometric method) 233.6, 234.3. $C_{10}H_9O_3SNa$. Calculated %: C 51.70; H 3.90; Na 9.90. M 232.2.

Decomposition of sulfonic acid (II). A mixture of 1.1 g of 91.86% sodium salt (II) and 50 g of 9.7% sodium hydroxide was refluxed for 6 hours. The naphthalene formed was washed out of the condenser with hot water and was filtered off after cooling the mixture. Yield 0.52 g (93.4%), m. p. 80°. The filtrate evolved sulfur dioxide on acidification.

On boiling a mixture of 1 g of sodium salt (II) and 100 g of a 15% sodium carbonate solution for 8 hours only traces of naphthalene were obtained; 0.73 g of the original material was isolated.

Refluxing a solution of 1 g of the sodium salt in 100 ml of 5% hydrochloric acid for 6.5 hours yielded 0.15 g of naphthalene.

4-Hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (III). A solution of 24.54 g of 94.62% sodium salt (II) in 125 ml of water was cooled rapidly and to the resulting suspension at 6° saturated bromine-water at 5-10° was added over a period of 1 hour up to the appearance of a stable reaction with starch-iodine paper (446 ml). 190 g of anhydrous sodium acetate was added to the solution at 20-25° and the sodium salt of (III) that separated was filtered and washed with alcohol. Yield 32.4 g.

The sodium salt of (III) crystallizes in tetragonal and hexagonal plates (from aqueous alcohol), dissolving readily in water and with difficulty in alcohol. Water of crystallization is lost slowly at ordinary temperatures over phosphorus pentoxide; at 100-110° it decomposes.

Found %: H_2O 9.82; C 32.80, 32.73; H 3.63, 3.81; Br 21.66, 21.52; Na 6.13, 6.08. $C_{10}H_{10}O_4BrSNa \cdot 2H_2O$. Calculated %: H_2O 9.87; C 32.89; H 3.86; Br 21.89; Na 6.30.

2-Bromonaphthalene. A mixture of 8 g of the bromo derivative (III) and 150 ml of 40% sulfuric acid was refluxed for 2 hours and the naphthalene and bromonaphthalene formed were distilled out with steam; 1.15 g of material of m. p. 50-53° and 1.65 g of m. p. 46-47° was obtained. To a solution of 1.45 g of the second fraction in 15 ml of alcohol a solution of 1.7 g of picric acid in 17 ml of alcohol was added and the precipitate that separated was filtered off after 24 hours (0.9 g, m. p. 100-137°). The filtrate was evaporated to dryness, the residue (2.1 g, m. p. 79.5-81°) was treated with sodium hydroxide and impure bromonaphthalene was steam-distilled out; 0.1 g of product of m. p. 46-47° and 0.97 g of m. p. 51-52° were obtained. The substance of m. p. 51-52° was recrystallized from alcohol in the form of plates of m. p. 54-55° that gave no melting point depression with 2-bromonaphthalene (m. p. 55°).

Naphthalene-2-sulfonic acid. To 150 ml of 10% sodium hydroxide at 95°, 5 g of the bromo derivative (III) was added in one lot and the solution was refluxed for 2 hours. The mixture was acidified with hydrochloric acid and evaporated to 110 ml. The precipitate that separated was filtered off and washed with alcohol. Yield 1.67 g (formation of naphthalene and sulfite was not observed).

The sodium salt consisted of tetragonal and hexagonal plates (from aqueous alcohol).

Found %: C 52.17, 52.18; H 2.90, 2.96; S 13.81, 13.72; $C_{10}H_7O_2SNa$. Calculated %: C 52.17; H 3.07; S 13.93.

The sulfonylchloride consisted of tetragonal and hexagonal plates (from acetic acid), m. p. 75.5-76.5°; it gave no melting point depression with naphthalene-2-sulfonylchloride (m. p. 75-76°).

The sulfonamide consisted of tetragonal and hexagonal plates (from alcohol) m. p. 215.5-216.5°; it gave no melting point depression with naphthalene-2-sulfonamide (m. p. 216-216.5°).

SUMMARY

1. On reacting 1-naphthol with bisulfite, 1,2- and 1,4-naphtholsulfonic acids are formed in addition to the bisulfite compound.

2. By reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid 1,2-dihydronaphthalene-2-sulfonic acid is obtained, together with other products.

3. 1,2-Dihydronaphthalene-2-sulfonic acid breaks down with alkalis and mineral acids to naphthalene and sulfurous acid, and is converted to 4-hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid by the action of bromine-water.

4. 4-Hydroxy-3-bromo-1,2,3,4-tetrahydronaphthalene-2-sulfonic acid gives naphthalene and 2-bromonaphthalene in acidic media and naphthalene-2-sulfonic acid in alkaline media.

5. The formation of 1,2-dihydronaphthalene-2-sulfonic acid on reduction of the bisulfite compound of 1-naphthol confirms the structure of the latter as 1-oxo-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (I).

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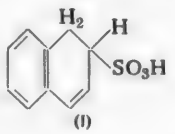
* Original Russian paginat on. See C. B. Translation.

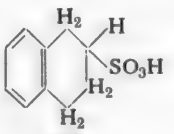
THE REDUCTION OF THE BISULFITE COMPOUND OF 1-NAPHTHOL AND ITS OXIME II

S. V. Bogdanov

It was recently reported [1] that by reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid a mixture of reaction products is formed, from which 1,2-dihydronaphthalene-2-sulfonic acid (I) was isolated. The precipitate that separated from the solution by the addition of sodium chloride contained 76.5% of the sodium salt of (I) and a considerable quantity of the sodium salt of a sulfonic acid that was inert to iodine and bromine-water and stable to alkalis and acids. It was separated from the main constituent (I) by fractional crystallization from water and boiling with 10% sodium hydroxide. From its composition and properties this compound is a tetrahydronaphthalenesulfonic acid and by dehydrogenation with sulfur it is converted to naphthalene-2-sulfonic acid; hence it can be surmised that it is the salt of 1,2,3,4-tetrahydronaphthalene-2-sulfonic acid (II). Judging by the composition of the salted out mixture of sulfonic acids the yield of the tetrahydronaphthalenesulfonic acid exceeds 11%. Its formation probably results from direct reduction of the bisulfite compound since compound (I) is stable to the action of zinc and acetic acid.



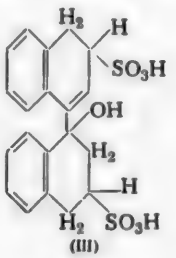
(I)



(II)

From the filtrate from the salted out mixture of salts (I) and (II) yet another substance was isolated in very small yield. On heating with 10% sodium hydroxide or 40% sulfuric acid it decomposes to 1,1'-dinaphthyl and sulfurous acid, and it reacts with bromine-water. This same compound was obtained in somewhat better yield (7%) by the reduction of the bisulfite compound of 1-naphthol with zinc and hydrochloric acid. The composition of this compound corresponds to the formula of the sodium salt of (1-hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III). Its formation probably proceeds through the corresponding pinacone.

The fission of (III) into 1,1'-dinaphthyl and sulfurous acid by the action of sodium hydroxide is effected in two stages. In the first stage, which proceeds fairly rapidly, the sodium salt of the monosulfonic acid, which is difficultly soluble in water, is formed; the second, slower stage leads to the dinaphthyl. An intermediate substance formed reacts with bromine-water and its composition corresponds to the sodium salt of (1-hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV).



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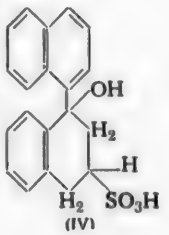

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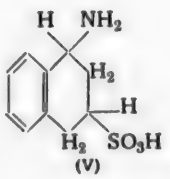

(V)

Reduction of 1,2,3,4-tetrahydronaphthalene-1-oxime with sodium in alcohol yields 1-amino-1,2,3,4-tetrahydronaphthalene [2]. It seemed interesting to carry out the reduction of the oxime of the bisulfite compound of 1-naphthol also. In this case, using zinc and dilute acetic acid in the presence of copper, a substance was obtained in 55% yield that was stable to alkalis and acids and the composition of which corresponded to 1-amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V). As side products, we detected the bisulfite compound of 1-naphthol, formed evidently by hydrolysis of the oxime group, and its reduction product – 1,2-dihydronaphthalene-2-sulfonic acid (I).

The course of the reduction of the bisulfite compound of 1-naphthol and its oxime, leading respectively to a mixture of (I), (II) and (III) and to (V) does not differ in principle from that of the reduction of 1-oxo-1,2,3,4-tetrahydronaphthalene and its oxime and confirms the structural formulas of the bisulfite compound of 1-naphthol and its oxime proposed previously [3].

EXPERIMENTAL

1,2,3,4-Tetrahydronaphthalene-2-sulfonic acid (II). A suspension of 22.7 g of a mixture of the sodium salts of sulfonic acids (II) and (I) [obtained by evaporating the filtrate from the first crystallization of the sodium salt of (I) and containing 29% of (I)] in 285 ml of 9.6% sodium hydroxide was refluxed for 7.5 hours; the bulk of the naphthalene formed from (I) was deposited in the reflux condenser. The mixture was diluted with water, acidified with hydrochloric acid and the solution evaporated to 225 ml. The precipitate was filtered off and washed with alcohol; yield 13.65 g. The product contained 3.6% of sulfonic acid (I) and was purified by recrystallizing from water.

The sodium salt of (II) consists of long, colorless tetragonal plates, dissolving readily in water and with difficulty in alcohol. It does not react with bromine or iodine in an acidic aqueous medium. It loses water of crystallization at 100-105°.

Found %: H_2O 7.05, 7.19. $C_{10}H_{11}O_3SNa \cdot H_2O$. Calculated %: H_2O 7.14. Found %: C 50.93, 51.02; H 4.65, 4.79; Na 9.66, 9.56. $C_{10}H_{11}O_3SNa$. Calculated % C 51.26; H 4.73; Na 9.82.

The sulfonyl chloride consists of long plates (from acetic acid), m. p. 72-73°; a mixture with naphthalene-2-sulfonyl chloride (m. p. 75-76°) melted at 50-53°.

Found %: Cl 14.99, 15.33. M (in benzene) 214.8, 221.7. $C_{10}H_{11}O_2ClS$. Calculated %: Cl 15.37. M 230.7.

The sulfonamide consists of tetragonal and hexagonal, thick plates (from alcohol), m. p. 142-143°.

Found %: N 6.59, 6.61. $C_{10}H_{13}O_2NS$. Calculated %: N 6.63.

Naphthalene-2-sulfonic acid. A mixture of 2.1 g of dry sodium salt of (III) and 1.15 g of sulfur was heated in a test tube in a metal bath, with frequent stirring, at 250° until evolution of hydrogen sulfide ceased (2.5 hours). The ground melt was extracted with hot water, the solution treated with charcoal, and evaporated to dryness. The residue was converted to the sulfonyl chloride and then to the sulfonamide.

The sulfonamide consists of tetragonal plates (from alcohol), m. p. 215.5-216.5° and gives no melting point depression with naphthalene-2-sulfonamide.

(1-Hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III). 1) The filtrate from the salted out mixture of sodium salts of (I) and (II), after the separation of zinc with sodium carbonate, was acidified with hydrochloric acid and evaporated on a water bath. The turbid liquid was decanted from the sodium chloride, deposited, and cooled. The precipitate formed was filtered off, the filtrate stirred with the sodium chloride deposited on evaporating, the liquid containing the suspended reduction products was decanted off, re-evaporated, etc. The reduction products and the naphthol bisulfite compound were contained in the residue filtered out. For the separation of (III) the mixture was crystallized from water; a fraction containing a considerable amount of (I) was discarded. From the total filtrates, corresponding to 1.36 moles of initial bisulfite compound 8.6 g of pure sodium salt of (III), 6.4 g of a mixture of the latter with the sodium salt of (II) and 9.2 g of a mixture of all three reduction products together with unchanged bisulfite compound, were isolated.

2) 31.5 g of zinc dust was added over a period of half an hour to a solution of 33.27 g of 89.5% bisulfite compound of 1-naphthol in 300 ml of water, acidified with 90 ml of 34.4% hydrochloric acid at 20-35°, and the

mixture was maintained for 4 hours at 50°. Evolution of hydrogen sulfide occurred during the reaction. Residual bisulfite compound, determined iodometrically, was 0.96-1.2%. In order to isolate the sodium salt of (III) the solution of reduction products, obtained from 0.24 moles of bisulfite compound, after precipitating the zinc with sodium carbonate and acidifying with hydrochloric acid, was evaporated to 520 ml and cooled. The precipitate (colorless needles and prisms) was filtered off and washed with alcohol; yield 9.4 g (7.7%).

The sodium salt consists of long, colorless prisms (from water), dissolving readily in water and with difficulty in alcohol. In contrast to (I), (II) and the original bisulfite compound, it forms a precipitate with silver nitrate (long, colorless prisms, soluble on heating). Under the conditions for the analysis of the bisulfite compound it does not take up iodine. It reacts with bromine in an acidic medium. Under the conditions for the determination of (I), particularly toward the end, the reaction goes very slowly and the solution immediately acquires a yellow color. A little more than 4 atoms of bromine are taken up by 1 molecule of the substance. It loses water of crystallization at 100°.

Found %: H_2O 5.65, 5.56. $C_{20}H_{18}O_7S_2Na_2 \cdot 1.5H_2O$. Calculated % H_2O 5.32. Found % C 49.43, 49.51; H 4.01, 3.91; S 13.23, 13.57; Na 9.44, 9.41. $C_{20}H_{18}O_7S_2Na_2$. Calculated % C 50.00; H 3.78; S 13.35; Na 9.58.

(1-Hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV) and 1,1'-dinaphthyl. A mixture of 5 g of the sodium salt of (III) and 350 ml of 9.8% sodium hydroxide was refluxed for 2 hours; after 45 minutes an almost transparent solution was formed but immediately the reaction products began to separate. The mixture was diluted with water, the precipitate filtered off and washed with water; the weight of reaction products was 3.75 g. On acidification the filtrate evolved sulfur dioxide. For separation of the sodium salt of (IV) and 1,1'-dinaphthyl, 7.5 g of the mixture was twice extracted with boiling water (200 ml each time). Sodium chloride was added to the filtrate and the sodium salt of (IV) that precipitated was filtered off and washed with water. The yield of dinaphthyl was 0.6 g and the sodium salt of (IV) – 6.68 g.

The sodium salt of (IV) consists of long, hexagonal plates (from water), dissolving with difficulty in cold water and considerably more readily in hot; it dissolves well in alcohol. Under the conditions for the determination of (I) it requires more than two atoms of bromine; the reaction goes very slowly toward the end and the solution acquires a brownish-yellow color. It loses water of crystallization over phosphorus pentoxide at room temperature.

Found %: H_2O 11.38, 11.49. $C_{20}H_{17}O_4SNa \cdot 2.5H_2O$. Calculated % H_2O 10.69. Found % C 64.45, 64.48; H 5.14, 4.64; Na 6.17, 6.00. $C_{20}H_{17}O_4SNa$. Calculated % C63.81; H 4.55; Na 6.11.

1,1'-Dinaphthyl. 1) A suspension of 2 g of the sodium salt of (III) in 100 ml of 40% sulfuric acid was refluxed for 3 hours. The mixture was diluted with water and the dinaphthyl was filtered off and washed with water; yield 0.9 g.

2) A mixture of 1 g of the sodium salt of (IV) and 70 ml of 9.8% sodium hydroxide was refluxed for 15 hours. The mixture was diluted with water and the dinaphthyl was filtered off and washed with boiling water to remove unchanged (IV); yield 0.45 g. On acidifying the filtrate sulfur dioxide was evolved. On substituting sodium hydroxide by 40% sulfuric acid the reaction proceeds at a considerably faster rate.

Thick tetragonal and hexagonal colorless plates or short prisms (from alcohol), m. p. 159.5-160°.

Found % C 94.36, 94.04; H 5.58, 5.49. M (in benzene) 241.2, 232.7. $C_{20}H_{14}$. Calculated % C 94.48; H 5.55, M 254.3.

1-Amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V). 10 g of zinc powder was added to a solution of 10.52 g of the oxime of the bisulfite compound of 1-naphthol and 1 g of copper sulfate in 100 ml of water acidified with 20 ml of 98% acetic acid, over a period of half an hour at 20-50°, and the mixture was maintained at 90° for 2 hours and then at 5° for 2 hours. The mixture of zinc and (V) was filtered off and (V) was extracted with a boiling sodium carbonate solution and precipitated with hydrochloric acid. A further quantity of (V) was isolated by evaporation of the main filtrate to 70 ml; its total yield was 5 g (55%). After further evaporation of the filtrate to 40 ml zinc acetate was filtered off and addition of sodium chloride to the filtrate yielded 0.5 g of the sodium salt of (I). The final filtrate contained (I) and the bisulfite compound of 1-naphthol.

Colorless, long plates and prisms, dissolving with difficulty in water and alcohol, does not contain water of crystallization. Remains unchanged on boiling with 9.7% sodium hydroxide and with 40% sulfuric acid.

The sodium salt is very readily soluble in water but is stable only in the presence of excess alkali.

Found %: C 52.78, 52.61; H 5.85, 5.74; N 6.15, 6.32; S 14.10, 14.32. $C_{10}H_{13}O_3NS$. Calculated %: C 52.84; H 5.77; N 6.16; S 14.10.

Benzoyl derivative. This was prepared from (V) and benzoyl chloride in the presence of sodium hydroxide. The sodium salt consists of colorless, long hexagonal, thin plates (from aqueous alcohol); dissolves readily in water and with difficulty in alcohol. Gives a precipitate with silver nitrate (colorless, long, hexagonal plates) soluble on heating. Loses water of crystallization at 100°.

Found %: H_2O 9.32, 9.31. $C_{17}H_{16}O_4NSNa \cdot 2H_2O$. Calculated %: H_2O 9.25. Found %: N 3.87, 3.83; Na 6.34, 6.33. $C_{17}H_{16}O_4NSNa$. Calculated %: N 3.96; Na 6.51.

SUMMARY

1. On reduction of the bisulfite compound of 1-naphthol with zinc and acetic acid, in addition to 1,2-dihydronaphthalene-2-sulfonic acid (I), 1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (II) and (1-hydroxy-1,2,3,4-tetrahydro)-(3',4'-dihydro)-1,1'-dinaphthyl-3,3'-disulfonic acid (III) are formed.

2. Compound (III) is obtained also when acetic acid is replaced by hydrochloric acid.

3. Compound (III) on heating with sodium hydroxide or with sulfuric acid is converted to 1,1'-dinaphthyl; in the case of sodium hydroxide,(1-hydroxy-1,2,3,4-tetrahydro)-1,1'-dinaphthyl-3-sulfonic acid (IV) is formed as an intermediate compound.

4. On reducing the oxime of the bisulfite compound of 1-naphthol with zinc and acetic acid,1-amino-1,2,3,4-tetrahydronaphthalene-3-sulfonic acid (V) is obtained.

5. The course of the reduction of the bisulfite compound of 1-naphthol and its oxime corresponds to that of the reduction of 1-hydroxy-1,2,3,4-tetrahydronaphthalene and its oxime and confirms the structural formulas of the bisulfite compound and its oxime proposed previously.

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ON THE SYNTHESIS OF CHOLINE AND THIOCHOLINE ESTERS OF CARBOXYLIC ACIDS

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The methods described in the literature for the preparation of choline and thiocholine esters of carboxylic acids are, as a rule, multistage processes and cannot meet the renewed requirements for these esters. For example, acetylthiocholine iodide is prepared by the multistage method of Renshaw [1]. Choline esters of carboxylic acids are synthesized by the action of acyl chlorides on choline chloride [2]. The synthesis of choline esters by the addition of 2-chloroethyl esters of carboxylic acids to trimethylamine in benzene solution by heating to 100° is described in the literature. By this means esters of choline chloride and stearic, palmitic, lauric, caprylic acids, etc. have been prepared. However, the isolation of individual products was not achieved by this means [3].

As has already been reported, we have developed a new method of synthesizing thioacetylcholine iodide [4] which comprises two stages – the preparation of 2-iodoethyl acetate and its addition to trimethylamine.

This method was used also for the synthesis of other acylthiocholine halides and also of acylcholine halides.

The initial esters of 2-haloalkylthiolcarboxylic acids and of 2-haloalkylcarboxylic acids are readily obtained by the action of haloanhydrides on alkylene sulfides [4] and correspondingly on the alkylene oxides according to the scheme:

$$R-\underset{\diagdown S \diagup}{CH}-CH_2 + R'COX \longrightarrow R-CHX-CH_2SCOR'$$

$$R-\underset{\diagdown O \diagup}{CH}-CH_2 + R'COX \longrightarrow R-\overset{OCOR'}{\overset{\diagup}{CH}}-CH_2X$$

The reaction proceeds during a short interval of time with the formation of the corresponding esters in 70% yield.

Acylthiocholine halides and acylcholine halides are prepared by addition of the 2-haloalkylthiolcarboxylic and 2-haloalkylcarboxylic esters to trimethylamine in the cold in a medium of dry ether according to the scheme:

$$(CH_3)_3N + XCH(R)CH_2SCOR' \longrightarrow (CH_3)_3\overset{+}{\underset{\bar{X}}{N}}CH(R)CH_2SCOR'$$

$$(CH_3)_3N + XCH_2CH(R)OCOR' \longrightarrow (CH_3)_3\overset{+}{\underset{\bar{X}}{N}}CH_2CH(R)OCOR'$$

The 2-iodoalkylthiolacyl and 2-iodoalkylacyl compounds combine with trimethylamine considerably more easily and with better yields of the corresponding thiocholine and choline carboxylic acid esters than do the 2-bromoalkylthiolacyl and bromoalkylacyl compounds.

Acetylthiocholine iodide [4], acetylthiocholine bromide, butyrylthiocholine bromide, 1-methylacetylthiocholine iodide and the oxygen analogs – acetylcholine iodide, acetylcholine bromide, benzoylcholine bromide, acetyl-2-methylcholine iodide and acetyl-2-methylcholine bromide were prepared by the above-described method.

By the addition of methyl 2-bromopropionate to trimethylamine, 3-methoxypropionyltrimethylammonium bromide was obtained.

Thus the previously developed method for the preparation of acetylthiocholine iodide is of a general nature and is applicable to the synthesis of other thiocholine and choline esters of carboxylic acids.

EXPERIMENTAL

Preparation of acetylthiocholine bromide. 9 g of 2-bromoethylthiol acetate and 20 ml of dry ether were placed in a round-bottomed flask. 3 g of trimethylamine was added gradually in small portions to the solution cooled to −15°. After each addition the flask was closed and shaken vigorously. At the end of the addition the flask was stoppered and left to stand in the cold for 4-5 hours and then for a further 2-3 days at room temperature.

The acetylthiocholine bromide formed as a precipitate was filtered off and crystallized twice from propyl alcohol. M. p. 213°. Yield 6 g (50%).

Found %: N 5.61; S 13.05; Br 33.1. $C_7H_{16}ONBrS$. Calculated %: N 5.79; S 13.2; Br 33.0.

The remaining thiocholine and choline esters of carboxylic acids were prepared similarly.

Preparation of butyrylthiocholine bromide. 15.5 g of 2-bromoethylthiol butyrate and 5 g of trimethylamine were taken for the reaction. The yield of butyrylthiocholine bromide was 9 g (45%). After recrystallizing twice from butyl alcohol the product melted at 140-143°.

Found %: S 12.0; Br 31.1; N 5.2. $C_9H_{20}ONBrS$. Calculated %: S 12.3; Br 30.7; N 5.4.

Preparation of acetyl-α-methyl-thiocholine iodide. For this preparation 14 g of 2-iodoisopropylthiol acetate and 3 g of trimethylamine were taken. 7.1 g (42%) of acetyl-α-methylthiocholine iodide was obtained. After recrystallizing twice from isopropyl alcohol the product melted at 231-235°.

Found %: S 10.2; I 35.5; N 4.3. $C_8H_{18}ONIS$. Calculated %: S 10.5; I 35.5; N 4.6.

Preparation of acetylcholine bromide. 10 g of 2-bromoethyl acetate and 3.5 g of trimethylamine were taken. The yield of acetylcholine bromide was 8.0 g (59%). After recrystallizing twice from ethanol the product melted at 143°.

Found %: Br 35.6; N 6.0. $C_7H_{16}O_2NBr$. Calculated %: Br 35.4; N 6.2.

Preparation of acetylcholine iodide. For this preparation 10.9 g of 2-iodoethyl acetate and 3 g of trimethylamine were taken. The yield was 9.1 g (65%). After recrystallizing twice from ethanol the product melted at 160-161°.

Found %: I 46.7; N 5.4. $C_7H_{16}O_2NI$. Calculated %: I 46.4; N 5.1.

Preparation of benzoylcholine bromide. 6 g of 2-bromoethyl benzoate and 1.7 g of trimethylamine were taken. The yield of benzoylcholine bromide was 4 g (52%). The product melted at 218°.

Found %: Br 31.21; N 5.35. $C_{12}H_{18}O_2NBr$. Calculated %: Br 31.0; N 5.42.

Preparation of acetyl-2-methylcholine bromide. For this preparation 16 g of 2-bromopropyl acetate and 5.5 g of trimethylamine were taken. The yield was 8.5 g (40%). M. p. 133-134°.

Found %: C 40.20; Br 33.50; N 5.65. $C_8H_{18}O_2NBr$. Calculated %: C 40.00; Br 33.35; N 5.83.

Preparation of acetyl-2-methylcholine iodide. 9.7 g of iodopropyl acetate and 2.5 g of trimethylamine were taken for the reaction. 8.0 g (66%) of acetyl-2-methylcholine iodide was obtained. M. p. 175°.

Found %: I 44.5; N 4.31. $C_8H_{18}O_2NI$. Calculated %: I 44.2; N 4.9.

Preparation of 3-methoxypropionyltrimethylammonium bromide. 15 g of methyl 2-bromopropionate and 5.3 g of trimethylamine were taken for the reaction. 13 g (65%) was obtained.

Found %: C 37.4; Br 35.45; N 6.0. $C_7H_{16}O_2NBr$. Calculated %: C 37.2; Br 35.4; N 6.2.

SUMMARY

1. It is shown that the method developed previously for the preparation of acetylthiocholine iodide is of general application for the synthesis of choline and thiocholine esters of carboxylic acids.

2. Acetylthiocholine bromide, butyrylthiocholine bromide, acetyl-2-methylcholine bromide, acetylcholine bromide, acetylcholine iodide, acetyl-2-methylcholine iodide, acetyl-2-methylthiocholine iodide, benzoylcholine bromide and 3-methoxypropionyltrimethylammonium bromide have been prepared by this method.

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REACTIONS OF AROMATIC NITRO COMPOUNDS

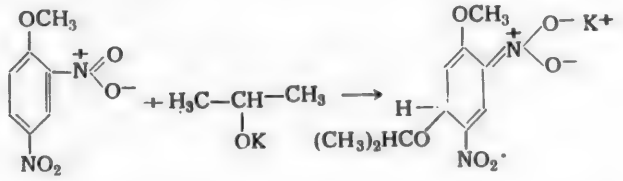
III. A NEW METHOD FOR THE PREPARATION OF ALKYL ETHERS OF 2,4-DINITROPHENOL

S. S. Gitis and A. I. Glaz

Up to the present time the synthesis of alkyl ethers of 2,4-dinitrophenol has been carried out by one of the following three methods – the reaction of the silver salt of 2,4-dinitrophenol with alkyl halides on heating [1-3], from 2,4-dinitrochlorobenzene on heating with alcohols and alkali [4] or with alcoholates [5]. According to Wesson [3] ethers of the above alcohols prepared from 2,4-dinitrochlorobenzene always contain the latter as an impurity. We have shown recently [6] that the methoxyl group in 2,4,6-trinitroanisole can be replaced easily by other alkoxyl groups. As a result of this we have carried out a number of investigations with 2,4-dinitroanisole also, with the object of converting it to other ethers. It was shown that this conversion takes place readily at room temperature. We assume that in this case also the reaction proceeds by the mechanism suggested in the previous communication [6].

By this means we prepared in good yield from 2,4-dinitroanisole the ethyl, n-propyl, n-butyl, isobutyl and isoamyl ethers of 2,4-dinitrophenol.

It is interesting to note that the isopropyl ether of 2,4-dinitrophenol could not be prepared by this method because the colored intermediate product is not decomposed by water. Evidently the branched isopropyl group does take up a position alongside the methoxyl group but goes to the position ortho to the nitro group in the fourth position, thus excluding the possibility of replacement of the methoxyl group.



Our method has a number of advantages over those described in the literature. The 2,4-dinitrophenyl ethers are obtained in the pure state and, without recrystallization, have constants almost identical with those in the literature.

The 2,4-dinitrophenyl alkyl ethers can be isolated from solution in the corresponding alcohols and in benzene. Carrying out the reaction in benzene solution has the advantage that the uptake of the alcohol is reduced 5-10 times and that of alkali is halved. Moreover the yield of the ethers is increased on the average by 10%.

Since the methods of preparation of the ethers in solution in the alcohols and in benzene do not differ in principle we will give details of only one of the syntheses.

EXPERIMENTAL

General method of preparing 2,4-dinitrophenyl ethers in benzene solution. 0.01 mole of 2,4-dinitroanisole was dissolved in 20 ml of benzene in the cold. To the solution was added 0.02 mole of potassium hydroxide dissolved by heating in 15-20 ml of the appropriate alcohol. The solution immediately acquired an orange-red color. After standing for an hour 50 ml of water was added to the solution and on shaking the color changed

to yellow. The benzene solution was washed three times with water after which 30 ml of water was added to it and a ternary mixture (benzene-alcohol-water) was distilled off. The ether which remained behind collected under the water in the form of heavy, oily drops. After cooling, the liquid esters were separated from water and redistilled in vacuo, and the solid esters were recrystallized from ethanol. The experimental results are given in the table.

Number	2,4-Dinitrophenyl ether	Yield (in %)	Properties	
			our data	literature data [3]
1	Ethyl	81	M. p. 85-86°	86°
2	n-Propyl	83	M. p. 29.5-30.5	30.5-31
3	n-Butyl	91	B. p. 161.5-162 (0.1 mm)	178-180 (2 mm)
4	Isobutyl	65	M. p. 30	30.3-31.5
5	Isoamyl	90	B. p. 168-170 (0.2 mm)	175-178 (1 mm)

SUMMARY

1. A new method is proposed for the preparation of higher alkyl ethers of 2,4-dinitrophenol.

2. The preparation of the 2,4-dinitrophenyl ethers confirms the mechanism previously put forward by us for the reaction between aromatic polynitro compounds and alcoholates.

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ON THE LIQUID-PHASE CATALYTIC CHLORINATION OF METHYLCHLOROSILANES

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The preparation of chloro derivatives of methylchlorosilane, dimethyldichlorosilane and trimethylchlorosilane by means of gaseous chlorine under ultraviolet light irradiation or with sulfuryl chloride in the presence of benzoyl peroxide has been described in sufficient detail in the literature [1].

The photochemical chlorination of methylchlorosilanes results in the formation of a mixture of chloro derivatives of varying degrees of chlorination [2], and it has been established that the chloromethyl group chlorinates more readily than the unsubstituted methyl group [3, 4]. In recent papers [5, 6] much attention has been given to vapor-phase photochlorination of methylchlorosilanes, which enables monochloro derivatives to be separated from the reaction zone.

The chlorination of organosilicon compounds in the presence of azodiisobutyronitrile has not been described in the literature. For this reason it seemed of interest to examine the suitability of this method of chlorination for the preparation of chloromethylchlorosilanes.

It would be expected that such a chlorination of methylchlorosilanes would proceed according to the known stepwise mechanism and lead to the formation of all possible methyl-group substitution products.

It was in fact established that depending on the molar ratio of methylchlorosilane to chlorine the complete range of chloro derivatives of CH_3SiCl_3, $(CH_3)_2SiCl_2$ and $(CH_3)_3SiCl$ with chlorine atoms in the methyl groups can be prepared, the same mechanism operating in this case as in the photochlorination of methylchlorosilane. The main factor determining the ratio of monochloro derivatives to polychlorides is the degree of conversion of the initial silane to its chloro derivatives and the ratio, determined by this, of the initial methylchlorosilane to monochloro derivative in the reaction mixture. In view of the fact that chlorine in the silane methyl group accelerates the rate of substitution on further chlorination, liquid-phase chlorination of methylchlorosilanes aimed at the preparation of monochloro derivatives must therefore result in a considerable amount of unreacted methylchlorosilane remaining in the reaction mixture.

The extent to which the chlorine reacts and the content of monochloro derivative in the reaction mixture, which is connected with this, is determined to a large extent by the nature of the initial methylchlorosilane.

Thus whereas in the case of $(CH_3)_3SiCl$ practically complete absorption of the chlorine takes place and the reaction product is practically free from dichlorides and has 30% of monochloro derivative in the mixture, on chlorination of CH_3SiCl_3 only 10% of the chlorine is used up under these conditions and dichlorides are present in the reaction mixture which contains only 4% of the monochloro derivative. On chlorinating $(CH_3)_2SiCl_2$ under similar conditions the uptake of chlorine and the content of monochloride in the mixture of reaction products reach 60% and 24.5% respectively and in this case dichloro derivatives were not detected. An increase in the degree of chlorination of the methylchlorosilanes leads to the appearance of di- and polychloro derivatives in the reaction product, the quantity of which increases in passing from $(CH_3)_3SiCl$ to CH_3SiCl_3, for $(CH_3)_3SiCl$ and $(CH_3)_2SiCl_2$ they constitute 17.6 and 31.5% of the product respectively (with a content of combined chlorine in the chlorination products of 45-48%), and for CH_3SiCl_3 – 53.4% (with 16% chlorine).

Expt. No.	Substance	Conditions of chlorination of methylchlorosilanes			Spec. grav. of react. mixt. after chlorination	Fract. comp. of react. mixt. after chlorination (%)				
		temp.	molar ratio			unchanged silane	monochloro-deriv.	di- and polychloro deriv.	residue	loss
			silane/Cl_2 in react. mixture	silane/Cl_2 reacted						
1	CH_3SiCl_3	50°	1 : 0.37	1 : 0.035	1.2912	92.4	4.0	—	2.5	1.1
2		60	1 : 0.53	1 : 0.16	1.3140	78.5	7.0	8.0	3.8	2.7
3		60	1 : 0.70	1 : 0.32	1.3378	67.2	4.5	21.3	4.0	3.0
4	$(CH_3)_2SiCl_2$	45—50	1 : 0.35	1 : 0.20	1.1326	67.4	24.5	—	4.5	3.6
5		50	1 : 0.50	1 : 0.45	1.1993	48.2	29.2	13.4	5.5	3.7
6		65—70	1 : 0.57	1 : 0.37	1.2173	55.1	20.1	13.3	6.2	5.3
7	$(CH_3)_3SiCl$	45—50	1 : 0.38	1 : 0.32	0.9778	69.0	31.8	2.8	3.0	2.4
8		45—50	1 : 0.50	1 : 0.48	0.9981	39.7	42.1	9.9	6.4	2.8
9		45—50	1 : 0.82	1 : 0.80	1.0654	13.3	48.1	28.6	7.0	3.0
10		45—50	1 : 0.91	1 : 0.90	1.1030	17.5	41.1	33.4	4.2	3.8

Note: The quantity of catalyst (on weight of silane) in experiments 1-7 was 0.3% and in experiments 8-10 – 0.2%.

In the catalytic chlorination of methylchlorosilanes as in the case of photochlorination of alkylchlorosilanes [7] an induction period (from 5 to 50 minutes) is observed at the beginning of the reaction.

Of the three methylchlorosilanes subjected to catalytic chlorination the most difficult to chlorinate is CH_3SiCl_3, this being shown by the longest induction period (up to 50 minutes), the highest rate of passage of chlorine throughout the entire chlorination process and the lowest degree of conversion of the initial silane to the chloro derivatives. The chlorination of $(CH_3)_3SiCl$ proceeds the most rapidly, the induction period being not longer than 5 minutes; the reactivity of $(CH_3)_2SiCl_2$ is intermediate between that of CH_3SiCl_3 and $(CH_3)_3SiCl$.

EXPERIMENTAL

Chlorination of the methylchlorosilanes was carried out in glass columns (height 220 mm, diameter 25 mm) fitted with a long, spiral, reflux condenser, a distributor (a sintered glass plate) for the introduction of chlorine and a thermometer. A current of dry, gaseous chlorine was passed into the mixture of the methylchlorosilane and catalyst at the chosen temperature. The catalyst was added at the beginning of the reaction and a further few times according to the falling off of the rate of evolution of HCl. At the end of the chlorination, dry air was passed through to remove dissolved HCl. Separation of the mixture was effected by multiple fractional distillation at atmospheric pressure in a flask with a herring-bone fractionating column (length 400 mm). The composition of intermediate fractions was calculated from the density. The experimental results are given in the table.

SUMMARY

1. The liquid-phase chlorination of the methylchlorosilanes – CH_3SiCl_3, $(CH_3)_2SiCl_2$ and $(CH_3)_3SiCl$ in the presence of azodiisobutyronitrile has been studied and it was established that by this method, depending on the molar ratio of silane to chlorine, the complete range of chloro derivatives containing chlorine atoms in the methyl group, can be obtained.

2. It was found that the same mechanism is operative in the liquid-phase catalytic chlorination of methylchlorosilanes as in photochlorination.

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IMPROVED METHODS OF SYNTHESIS OF PHENYLDICHLOROPHOSPHINE AND PHENYLPHOSPHINIC DICHLOROANHYDRIDE

E. L. Gefter

Phenyldichlorophosphine and phenylphosphinic dichloroanhydride are important intermediate products for the synthesis of various classes of aromatic organophosphorus compounds. However the methods of preparation of these chloroanhydrides (particularly of the first) have various deficiencies. Phenyldichlorophosphine can be prepared by several methods [1], two of which are of practical significance. 1) By the interaction of benzene and phosphorus trichloride in the gaseous phase [1]. This method requires cumbersome apparatus and a long continuous process; moreover there is always a substantial danger of fire and explosion. 2) By the interaction of benzene and phosphorus trichloride in the presence of aluminum chloride [1, 2]. This method is considerably simpler but on the negative side there is the necessity for complexing the catalyst before isolating the phenyldichlorophosphine (without this it is impossible to achieve good yields of the product) which is a troublesome and sometimes even a hazardous operation [2]. The maximum yield of phenyldichlorophosphine by the second method is 78% [2].

Phenylphosphinic dichloroanhydride can be synthesized by the oxidation of phenyldichlorophosphine with oxygen (a very dangerous method), with chlorine and phosphorus pentachloride, by the partial hydrolysis of phenyltetrachlorophosphine or by treating it with sulfur dioxide and finally by the interaction of phenylphosphinic acid with phosphorus pentachloride [1].

In the course of work on the development of more convenient and acceptable methods of synthesis of the two chloroanhydrides in question we have found that phenyldichlorophosphine can be prepared very simply, in complete safety and in better yields than those reported in the literature if after reacting benzene and phosphorus trichloride in the presence of aluminum chloride (in the molar ratios 1:3:1) the catalyst is combined with pyridine and the phenyldichlorophosphine is vacuum-distilled directly from the reaction flask. The yield of phenyldichlorophosphine is about 90% [3].

By treatment of phenyldichlorophosphine with chlorine, phenyltetrachlorophosphine was obtained and the latter (without isolation) gave phenylphosphinic dichloroanhydride in a yield of about 90% by reaction with sulfur dioxide. The general scheme of preparation of the two chloroanhydrides is indicated below.

$$C_6H_6 + 3PCl_3 + AlCl_3 \longrightarrow C_6H_5PCl_2 \cdot AlCl_3 + 2PCl_3 + HCl$$

$$C_6H_5PCl_2 \cdot AlCl_3 \xrightarrow{C_5H_5N} C_6H_5PCl_2 + AlCl_3 \cdot C_5H_5N \quad (1)$$

$$C_6H_5PCl_2 + Cl_2 \longrightarrow C_6H_5PCl_4 \xrightarrow{SO_2} C_6H_5POCl_2 + SOCl_2 \quad (2)$$

EXPERIMENTAL

Phenyldichlorophosphine. In a four-necked, round-bottomed flask fitted with a dropping-funnel, a reflux condenser with a calcium chloride tube, a sealed stirrer and a thermometer, 39 g of benzene, 206 g of phosphorus trichloride and 70 g of aluminum chloride (molar ratios 1:3:1) were mixed. The mixture was refluxed for 3 hours with vigorous stirring. The hydrochloric acid which was copiously evolved was absorbed in water. The mixture was then cooled and the excess phosphorus trichloride was distilled off at 30-40 mm at a bath temperature of 50-55°. To the viscous, liquid residue 42 g of dry pyridine (molar ratio $AlCl_3:C_5H_5N = 1:1$) was added

with stirring, the reaction temperature being maintained at 40-50° by external cooling. The product obtained, which solidifies below 60-70°, was heated above its melting point and distilled in vacuo, with stirring, at 2-3 mm and a bath temperature of 90-155°, a low-boiling fraction being taken off first, followed by 83 g of crude phenyldichlorophosphine. After repeated redistillation 80 g (90%) of pure phenyldichlorophosphine was obtained, having b.p. 58-59° at 0.8-1 mm, $n^{20}D$ 1.5960, d^{20}_4 1.3191, in conformity with the data in the literature [2]. On increasing the quantities of starting materials 12 times, the yield of phenyldichlorophosphine was 85-87%.

Phenylphosphinic dichloroanhydride. In a four-necked, round-bottomed flask fitted with a reflux condenser with a calcium chloride tube, a stirrer, a thermometer and a gas inlet tube was placed 1720 g of phenyldichlorophosphine dissolved in 1400 ml of carbon tetrachloride. The gas inlet tube was placed above the surface of the liquid and dry chlorine was passed through the system, with thorough stirring of the mixture. The reaction temperature was kept between the temperature limits of 10-20° by external cooling. The phenyltetrachlorophosphine precipitated in the form of yellowish-white crystals. After the exothermic reaction ceased (8 hours) chlorine was passed for a further 5-10 minutes; then the gas inlet tube was submerged in the semiliquid mass and dry, gaseous sulfur dioxide was passed into the system at 5-15° (again with stirring and external cooling) until the crystals completely disappeared and the reaction mixture was converted to a homogeneous yellow liquid. A low-boiling fraction was distilled off (SO_2, $SOCl_2$, SO_2Cl_2, CCl_4) and the residue was redistilled at 83-84° (1 mm). 1650 g (90%) of phenylphosphinic dichloroanhydride was obtained; $n^{20}D$ 1.5578, d^{20}_4 1.1977, in conformity with the data in the literature [1].

SUMMARY

Simple methods for the synthesis of phenyldichlorophosphine and phenylphosphinic dichloroanhydride in yields of about 90% of theory have been developed.

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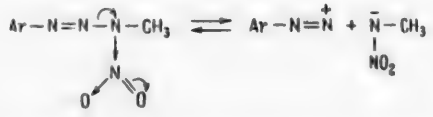
THE STRUCTURE AND TRANSFORMATIONS OF METHYLARYL-N-NITROTRIAZENES

III. ON SOME PROPERTIES OF METHYLARYL-N-NITROTRIAZENES

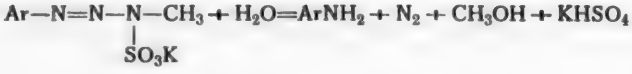
N. M. Baranchik, I. V. Grachev and D. Z. Zavel'skii

A study of the properties of methylaryl-N-nitrotriazenes has shown that the splitting of these compounds into their initial components takes place not only in acidic media as for methylaryl-N-triazenesulfonic acids [2, 3], but also in neutral media since the nitro group, being a more powerful electrophilic substituent than the sulfonic acid group polarizes the bond between the diazo and the amino components more strongly.



(I)

For the same reason it would be expected that the elimination of acyl groups in acidic media, characteristic of N-triazenesulfonic acids [3]



(II)

should occur more strongly in N-nitrotriazenes. However, investigations carried out in the present paper have shown that in media of pH from 1 to 7 at room temperature N-nitrotriazenes do not split off the slightest trace of nitric acid even over a period of 6 weeks. The same results are also shown on heating N-nitrotriazenes to boiling point in 68% sulfuric acid.

The unexpected strength of the bonds between nitro groups and the amino nitrogen of triazenes in acidic media, in comparison with the corresponding bonds in the case of sulfonic acid groups can, we suggest, be explained in the first place by the fact that the polarity of the bond between the two different elements, nitrogen and sulfur, is stronger than that between two nitrogens. In addition one should take into account Sidgwick's view [4] that in the bond between two nitrogens the two atoms evidently share a lone electron pair and this imparts additional strength to such bonds. The basis for this assumption is, according to Sidgwick, the fact that the heat of formation of an N=N bond is 2.54 times greater and of an N≡N bond 5.86 times greater than that of an ordinary N–N bond whereas the heat of formation of a C=C bond is only 1.79 times and of a C≡C bond 2.35 times greater than that of an ordinary C–C bond.

The tendency of a double bond between nitrogen atoms to be converted to a triple bond, with elimination of nitrogen is well known.

A similar tendency of a single bond between nitrogen atoms to be converted to a multiple bond can be observed in the action of acids on nitramines, and in particular, on methylnitramine. It was shown [5] that in this case nitrous oxide and methyl alcohol is formed.

$$CH_3—NH—NO_2 \longrightarrow N_2O + CH_3OH \quad \text{(III)}$$

The action of acidic media on methylaryl-N-nitrotriazenes is exactly the same. Fission to the initial components first takes place according to reaction (I), which is favored by the strongly electrophilic nature of the nitro group, and the methylnitramine breaks down according to reaction (III).

We found an even greater difference between the properties of methylaryl-N-nitrotriazenes and methylaryl-N-triazenesulfonic acids in a study of the action of different alkalis and basic organic solvents on methylaryl-N-nitrotriazenes.

It has been reported previously [1] that N-nitrotriazenes cannot be recrystallized from such solvents as alcohol, benzene ether, etc. because they decompose during the process, with the evolution of gas. We have now found that N-nitrotriazenes dissolve readily in pyridine and somewhat less easily in triethylamine and certain other basic solvents. It was found that the solutions are colored, in the case of pyridine a deep red-brown and in triethylamine a bright orange.

Freshly prepared solutions of N-nitrotriazenes in basic solvents precipitate the unchanged initial materials on dilution with water. If however these solutions are allowed to stand for a few hours the N-nitrotriazenes do not separate on dilution, and on acidification of the dilute aqueous solutions diazo compounds and nitrous acid are found in considerable quantities.

It was shown that N-nitrotriazenes give orange-colored solutions in aqueous ammonia also. On keeping for 6 weeks at room temperature these solutions deposit crystals that prove to be the arylamines and diazo compounds that enter into the composition of the N-nitrotriazenes undergoing decomposition in the ammonia solution. In aqueous alkali solutions N-nitrotriazenes dissolve with a red or cherry color. If such solutions are kept for some time and are then extracted with ether, the extract, after removal of the ether, again contains arylamines. If the arylamine in question is volatile it can be isolated from the original solution in a fairly pure state, by steam distillation. Diazo compounds and nitrous acid are found on acidification of the solution remaining after extraction with ether or steam distillation.

The reactions described take place even more clearly in alcoholic potassium hydroxide solutions. N-nitramines dissolve readily in these with a deep cherry color. On diluting the solutions with a saturated, aqueous bicarbonate solution the N-nitrotriazene dissolved precipitates unchanged and after standing for 12 hours at room temperature, 32-34% of the arylamine and 31.5-32.5% of the sodium nitrite theoretically possible, as calculated from the initial triazene, can be isolated from the solutions,

Most characteristic is the behavior of nitrotriazenes in sodium methylate solutions. For example, a solution of a triazene in methanol containing 1.2% CH_3ONa, on standing for 15 minutes after dissolving the triazene, precipitates 52% of the unchanged initial material on addition of water and bicarbonate. After 30 minutes only 35%, and after an hour only 13%, of the triazene can be recovered. Together with it correspondingly more amine and nitrite are found. Finally, 30.5% sodium methylate, within 1.5-2.0 hours after dissolving a nitrotriazene, brings about 76-78% conversion of the latter to the amine and 85% to nitrite.

Further investigation showed that in addition to the amine and nitrite, among the decomposition products formaldehyde can be detected; this was identified by its characteristic reactions with phenylhydrazine and sodium nitroprusside and also with phenylhydrazine and potassium ferricyanide. Quantitative analysis by means of hydroxylamine hydrochloride showed that the decomposition products of an N-nitrotriazene in a 16.5% sodium methylate solution, on standing for 1.5-2.0 hours contains 54-59% of the formaldehyde theoretically possible. At the same time under these conditions 43% of the arylamine and 53.5% of the nitrite was found.

It was observed that on allowing solutions of methylaryl-N-nitrotriazenes and sodium methylate to stand their dark-cherry color changes to brown but no gas is evolved. On adding aqueous bicarbonate to these solutions until there is no reaction for free sodium hydroxide (to thiazole paper) evolution of nitrogen is observed and this becomes more vigorous on heating.

Thus it was found that methylaryl-N-nitrotriazenes, containing no hydrogen attached to oxygen or nitrogen, which are normally pale-yellow in color dissolve in aqueous or alcoholic alkalis and in sodium methylate, giving

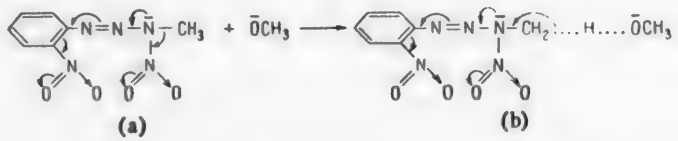
bright-red or dark-brown solutions, and in pyridine, triethylamine and ammonia – dark-brown or orange solutions. On allowing the alkaline, and in particular the methylate, solutions to stand, their color changes and the methylaryl-N-nitrotriazenes dissolved undergo decomposition with the formation of arylamines, nitrite, formaldehyde and nitrogen. The arylamines formed in this way correspond in structure to the diazo compounds from which the triazene was synthesized.

This decomposition reaction can be depicted by the following

$$Ar{-}N{=}N{-}\underset{\displaystyle NO_2}{\overset{|}{N}}{-}CH_3 + H_2O = ArNH_2 + N_2 + CH_2O + HNO_2 \qquad (IV)$$

In view of the inclusion of a molecule of water on the left side of the above equation this might have been considered to be a hydrolytic reaction. However, a more thoughtful examination shows that as a result of the reaction two component parts of the methylaryl-N-nitrotriazene, namely the diazo compound and the nitro group, are reduced to the amine and nitrous acid, and two other components, the methyl group and the two substituted nitrogens, are oxidized to formaldehyde and nitrogen.

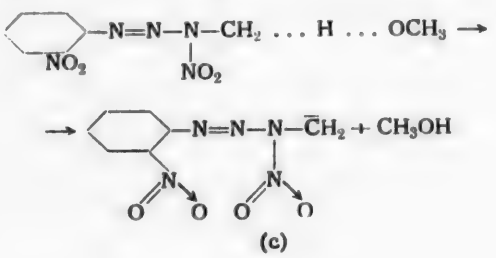
We consider that the reaction observed can be explained by the following considerations. In the methylaryl-N-triazenes the amino nitrogen to which the methyl group is attached is at the same time connected to two electrophilic substituents – the nitro group and the arylazo group; the methyl group also contains electrophilic substituents. Under the influence of these groups, which is transmitted through the amino nitrogen, the hydrogen of the methyl group acquires a marked acidic character. In solutions of alkalis, particularly of sodium methylate, the methyl group begins to split off a proton as a result of attack by the methylate anion.



(V)

This results in a marked increase of the displacement of electrons toward the two electrophilic substituents because of the increased electron density on the carbon of the methyl group. A shift of part of the charge toward the nitro and arylazo groups naturally brings about a bathochromic effect, which is shown by the deep red color of methylate solutions of a methylaryl-N-nitrotriazene.

After the transition state (b) is broken down by complete removal of the proton (VI) the anion (c) is formed which cannot be stabilized in the form of the hypothetical compound (d) since the nitrogen next to the methylene group would have 10 electrons. Stabilization occurs by elimination of the nitro group (VII) which is converted to a nitrite anion by addition of the excess electron pair from the imino nitrogen, and the formation of the methylene derivative of o-nitrophenyltriazene (e)



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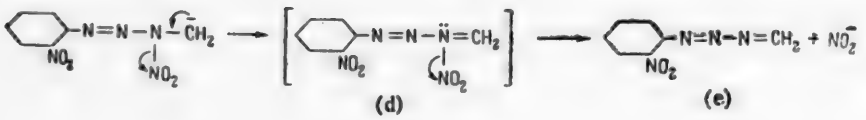
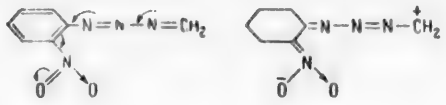
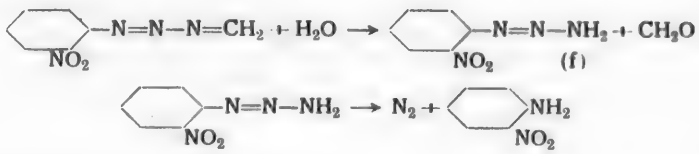


(VII)

Compound (e) would no longer be likely to be deeply colored because its bipolar structure would be too strained.

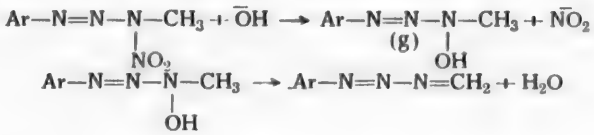


When the methylate solution, after standing, is diluted with water, acidified and heated, the azomethine (e) breaks down (VIII) into formaldehyde and the o-nitrophenyltriazene (f). The latter, being analogous to the extremely labile phenyltriazenes studied previously by Dimroth [6], breaks down to nitrogen and o-nitroaniline.



(VIII)

It was also suggested that the reaction under investigation proceeds possibly not through stages (V), (VI) and (VII) but through stages (X) and (XI).

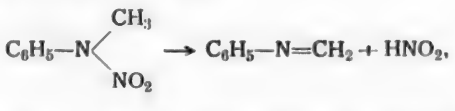


(X)

(XI)

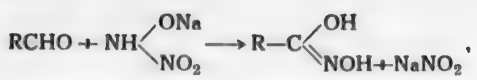
In this case after replacement of the nitro group, which splits off as a nitrite ion, the arylazo-substituted methylhydroxylamine (g) must be formed. Such compounds were synthesized by Bamberger and his co-workers by the condensation of diazo compounds with methylhydroxylamine [7]. These N-hydroxytriazenes give in alcoholic solution a characteristic greenish-blue coloration with ferric chloride but split off water by the action of alkalis, with formation of azomethines. However, among the decomposition products of various methylaryl-N-nitrotriazenes in alcoholic alkali we never succeeded in detecting even traces of N-hydroxytriazenes. Hence this reaction proceeds through stages (V), (VI) and (VII).

It should be borne in mind that Bamberger [8], while studying the properties of arylnitramines, which he called diazobenzenic acids, found that on refluxing phenylmethylnitramine, or its p-nitro derivative, with aqueous-alcoholic alkali for 40 hours, the arylamine, nitrite and formic acid were formed in considerable quantity. The author represented this reaction in the following way:



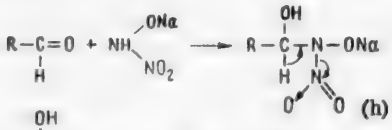
and suggested that the formic acid found is a product of the Canizzaro reaction between formaldehyde and alkali, although he did not confirm the presence of methyl alcohol. Franchimont and van Erp [9] observed a similar reaction for aliphatic methylnitramines. However, the elimination of the nitro group in the cases of the authors mentioned took place with much more difficulty than in the case described by us.

In many textbooks of organic and analytical chemistry [10] the Angeli reaction [11] is given as a method of determination of aldehydes. It involves the fact that by the action of aldehydes on the sodium salt of nitrohydroxylamine in aqueous solution, hydroxamic acid is formed, which gives a characteristic, intense red color with ferric chloride. This reaction can be represented by the following equation:

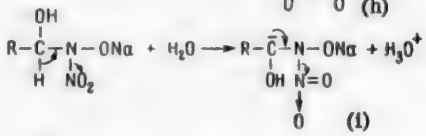


though Shlenk and Bergman [10] point out that the stages of this reaction are not clear.

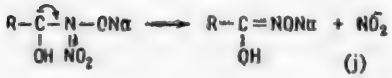
We consider that the Angeli reaction can be depicted by the following stages



(XII)



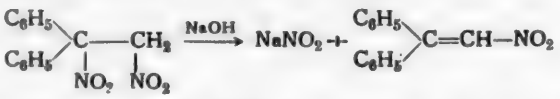
(XIII)

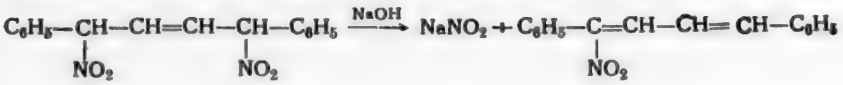


(XIV)

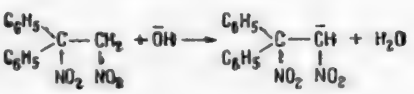
In this case the elimination of a proton from the carbon (XIII) of the addition product (XII) of the aldehyde and nitrohydroxylamine (h) takes place more easily because there is already a hydroxyl group in it. The carbanion (i) that is formed is stabilized further by elimination of the nitro group in the form of a nitrite ion, and the formation of hydroxamic acid (j).

Our proposed reaction mechanism seems to us to explain satisfactorily all reactions whereby aliphatic C-nitro compounds split off the nitro group in the form of a nitrite ion in alkaline media, and undergo intramolecular re-arrangement of the bonds. For example, Wieland [12] found that α,α-diphenyl-α,β-dinitroethane and 1,4-diphenyl-1,4-dinitrobutene split off nitrous acid in alkaline media with the formation of the corresponding α,α-diphenyl-β-nitroethylene and 1,4-diphenyl-1-nitrobutadiene-1,3

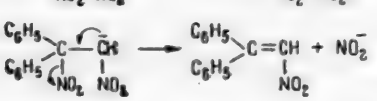




This seemingly strange reaction can easily be explained in the following way:



(XV)



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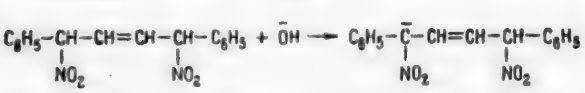
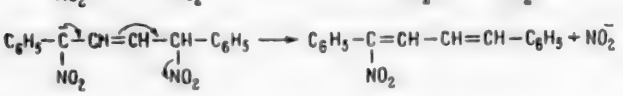


(XVII)



(XVIII)

In the first place a proton splits off from the pseudo-acid under the action of the alkaline medium and the carbanion formed becomes stabilized by the formation of a double bond with the neighboring atom, suitable regrouping of other bonds and elimination of a nitro group in the form of a nitrite ion.

The reactions examined above must be considered as belonging to the series of nucleophilic elimination reactions studied in detail by Ingold, Hughes and others [13], taking the example of the interaction of alkyl halides and quaternary ammonium salts with alkalis. A detailed review of the mechanism of these reactions has been made by Reutov [14].

EXPERIMENTAL

Behavior of 1-methyl-1-nitro-3-aryltriazenes in basic solutions. 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene dissolves readily in pyridine in the cold and still better on moderate heating. A solution of an intense red-brown color is thereby obtained. On cooling the freshly prepared solution in ice, or on diluting with water, a light-yellow crystalline precipitate of the original triazene separates.

TABLE 1

Decomposition of an N-nitrotriazene in 1.2% CH_3ONa Solution

Time of standing of solution (in minutes)	Unchanged triazene isolated (in % of original)	Diazo compound found in triazene decomposition products (in %)
15	52	30
	52	29
30	35	43
	30	37
60	13	43

The original triazene already fails to separate, on dilution with water, from a solution of the N-nitrotriazene in pyridine which has been kept for a few hours. On diluting with water and acidifying a pyridine solution of the triazene kept for 3-4 hours, nitrous acid (positive reaction with starch-iodine paper) and 2-nitrodiazobenzene (coupling with β-naphthol and determination of the azo dye formed) are detected in it. On similar treatment of a pyridine solution of the triazene kept for 24 hours, nitrous acid and the diazo compound are no longer detectable.

The N-nitrotriazene dissolves in triethylamine with more difficulty than in pyridine. Heating accelerates solution. The color of the solution is bright orange. On cooling the freshly prepared solution, crystals of the original triazene separate. The diazo compound can be detected on diluting with water and acidifying the triethylamine solution, after keeping the latter for a time.

Other methylaryl-N-nitrotriazenes behave similarly, including that obtained from 2,5-dichlorodiazobenzene, i.e., one not containing a nitro group on the aryl nucleus.

Behavior of 1-methyl-1-nitro-3-aryltriazenes in aqueous alkaline solutions. 0.5 g of 1-methyl-1-nitro-3-(2'-nitrophenyl)-triazene was added to 100 ml of 10% sodium hydroxide solution. In the cold the powder was not wetted. On heating to boiling the powder darkened and formed a suspension and finally rose to the surface in the form of a dark, fused resin. The solution acquired a red coloration during this treatment. After 5 days the reaction products were removed by steam distillation. Orange crystals of m. p. 69-70° (from alcohol) were isolated from the distillate by ether extraction. A mixture with authentic 2-nitroaniline (m. p. 72°) showed no melting point depression.

The suspension left after steam distillation was filtered and the filtrate was divided into two equal portions. o-Nitroaniline was isolated from the first half of the filtrate by ether extraction, since by treatment with nitrite in an acid medium it gave a diazo compound which formed azo dyes with R-salt and β-naphthol identical with those obtained from authentic o-nitrodiazobenzene.

The second half of the filtrate was acidified with hydrochloric acid, whereupon the solution became colorless. The acidified solution contained the diazo compound (coupling with β-naphthol) and nitrous acid (qualitative test with starch-iodine paper and with metanil-yellow).

1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene behaves similarly with sodium and potassium hydroxide solutions at other concentrations.

TABLE 2

Formation of o-Nitroaniline on Decomposition of 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene in Sodium Methylate Solutions of Various Concentrations

Content of CH_3ONa in solution (in %)	Quantity of amine found (in %)
2.4	6.2
	6.7
9.5	7.1
16.5	43.2
	38.9
21.0	58.0
	58.8
26.0	76.2
	74.7
	76.5
30.5	78.1
	76.4

TABLE 3

Formation of Nitrite on Decomposition of 1-Methyl-1-nitro-3-(2'-nitrophenyl)-triazene in Sodium Methylate Solutions of Various Concentrations

Content of CH_3ONa in solution (in %)	Quantity of nitrite found (in %)
9.5	26.4
16.5	53.5
21.0	66.1
26.0	84.5
30.5	85.6

1-Methyl-1-nitro-3-(4'-nitrophenyl)-triazene dissolves in aqueous alkali solutions to give a cherry color. Ether extraction or steam distillation of alkaline solutions of the N-nitrotriazene after long standing yield p-nitroaniline, the diazo compound of which is a component for the synthesis of the original methyl-aryl-N-nitrotriazene.

If alkaline solutions of the N-nitrotriazene are acidified the diazo compound can be detected in them. If again the alkaline solutions are acidified after previous removal of p-nitroaniline by ether extraction or steam distillation, nitrous acid is found in addition to the diazo compound.

0.001 mole of 1-methyl-1-nitro-3-(4'-chloro-2'-nitrophenyl)-triazene was dissolved in 100 ml of 25% ammonia. The orange solution formed was kept at room temperature for 6 weeks. Crystals of m. p. 94° were formed at the bottom of the flask. After recrystallizing from alcohol they had m. p. 114-115° (4-chloro-2-nitroaniline melts at 116-117°). On treatment with nitrite in an acid medium the crystals formed 4-chloro-2-nitrodiazobenzene which was identified through the azo dyes formed by coupling with β-naphthol and R-salt.

Decomposition of methylaryl-N-nitrotriazenes in alcoholic alkali. 0.23 g of o-nitrophenylmethyl-N-nitrotriazene was dissolved in a 12% solution of potassium hydroxide in ethyl alcohol. To the transparent, dark-cherry colored solution a dilute aqueous bicarbonate solution was added gradually, with cooling; the color then changed to yellow, a turbidity appeared and nitrogen was evolved. The alcohol was distilled off in vacuo. The residual aqueous solution was extracted with ether until a fresh portion of ether did not become colored and a test portion of the aqueous solution continued to give a positive diazo reaction on acidification. The residue from the extract after removal of the ether was dissolved in hydrochloric acid and back-titrated with nitrite.

For determination of the nitrite content of the bicarbonate solution the latter after extraction with ether was added dropwise to an accurately weighed quantity of sulfamic acid, dissolved in 50 ml of 10% sulfuric acid, and the excess sulfamic acid was back-titrated with 0.1 N nitrite solution.

In two similar experiments 33.8 and 31.6% of the amine and 32.4 and 31.5% of the nitrite theoretically possible, was found. If the N-nitrotriazene is dissolved in alcoholic potassium hydroxide, diluted with water immediately and neutralized with bicarbonate, the nitrotriazene is recovered practically unchanged. (4-Chloro-2-nitrophenyl)-methyl-N-nitrotriazene also decomposes in alcoholic potassium hydroxide with the formation of the amine and nitrite.

Decomposition of methylaryl-N-nitrotriazenes in sodium methylate. To 0.001 mole N-nitrotriazene, accurately weighed, 20 ml of sodium methylate solution was added. Complete solution was effected in 5-10 minutes on shaking the stoppered flask. Sodium methylate in the following concentrations was used: 1.2, 2.4, 9.5, 16.5, 21.0, 26.0 and 30.5%. In the methylate solutions of strengths from 16.5 to 30.5% the triazene dissolved

with a characteristic deep red cherry color. In the solutions of lower concentration an increasingly brown color was formed.

The above-mentioned coloration in sodium methylate is characteristic not only of methylaryl-N-nitrotriazenes containing a nitro group on the aryl nucleus but also of the N-nitrotriazene obtained from 2,5-dichlorodiazobenzene.

The behavior of solutions of methylaryl-N-nitrotriazenes in sodium methylate will be described below from the example of 1-methyl-1-nitro-3-(2'-nitrophenyl)-triazene.

Process of decomposition of a triazene in sodium methylate. A solution of the N-nitrotriazene in a 1.2% solution of sodium methylate was allowed to stand at room temperature for 15 minutes to 1 hour. The solution was then added dropwise, with good stirring, to 20 ml of 10% sulfuric acid cooled to 0-3° with ice. Light-yellow flakes separated out of the solution immediately. The suspension formed was filtered off rapidly on a sintered-glass filter, the solid product washed with ice-water, sucked off at the pump and dried in a vacuum desiccator to constant weight. The dried precipitate is a light-yellow powder showing the properties of N-nitrotriazenes: it has no clear melting point and ignites on moderate heating; with α-naphthylamine in glacial acetic acid it forms a brightly colored solution of the azo dye; in an alcoholic solution of β-naphthol crystals of the β-naphthol azo dye gradually precipitate.

The filtrate after separation of the unchanged triazene was analyzed for the quantity of diazo compound formed on pouring the methylate solution of the partially decomposed triazene into the acid. 20 ml of a 0.1 N alcoholic solution of β-naphthol, 30 ml of a concentrated acetate buffer solution and then bicarbonate to pH 6-7, were added to the filtrate with stirring. The excess β-naphthol, not used up in azo coupling, was back-titrated with a 0.1 N p-nitrophenyldiazonium salt solution. The analytical data are given in Table 1.

Determination of o-nitroaniline in the triazene decomposition products. a) A solution of the triazene in 21-26% sodium methylate after standing 1-2 hours was diluted with water and steam distilled. From the turbid, yellow distillate crystals of m. p. 70-71° (decomp.) were isolated. A mixed melting point with authentic o-nitroaniline showed no depression.

b) To a solution of the triazene in 21-26% sodium methylate, kept for 1.5-2.0 hours at room temperature, was added with cooling, first water and then saturated bicarbonate solution. The yellow solution which became turbid and evolved gas, was extracted with ether. Crystals of impure o-nitroaniline, which required several recrystallizations for purification, were isolated from the ether.

On treating the residue obtained from the ether extract with warm 20% hydrochloric acid the o-nitroaniline dissolves completely and a yellow-orange crystalline material is found in the solid residue. This substance when dissolved in α-naphthylamine, on heating (especially in the presence of a few drops of concentrated hydrochloric acid) gives the bright color characteristic of o-nitrophenylazo-β-naphthol in acetic acid. Hence it is the diazoamino compound, based on o-nitrodiazobenzene. The crude material (m. p. 177-180°) after recrystallizing from benzene and alcohol melted at 192°. It gave no melting point depression when mixed with 2,2'-dinitrodiazoaminobenzene (m. p. 195-196°). Hence, on neutralizing a solution of the triazene in sodium methylate, with bicarbonate, 2,2'-dinitrodiazoaminobenzene is formed in addition to o-nitroaniline.

c) To a solution of the triazene in sodium methylate, after standing for 1.5-2 hours at room temperature, 20 ml of a saturated solution of sodium bicarbonate was added. The reaction mixture changed color toward yellow, this effect being more marked at lower sodium methylate concentrations. The excess methyl alcohol was removed by heating on a water-bath at 30-35° for 30 minutes at reduced pressure.

After removal of the alcohol the solution was extracted with several portions of ether, the total volume of which was about 200 ml; the ether was distilled off on the water-bath and the residue treated with 50 ml of hot hydrochloric acid (d 1.12). The hydrochloric acid solution was diluted with water, cooled and titrated with 0.1 N sodium nitrite solution, the titer of which was determined by means of sulfamic acid.

The results of experiments on the determination of the quantities of o-nitroaniline formed on the decomposition of the triazene (sample weight 0.222-0.229 g) in sodium methylate solutions of various concentrations, are given in Table 2.

From the data of Table 2 it is seen that with increasing concentration of CH_3ONa in the solution, the extent

to wnich the N-nitrotriazene decomposes with the formation of o-nitroaniline also increases.

Determination of nitrous acid in the triazene decomposition products. To a solution of the triazene (about 0.224-0.227 g) in a sodium methylate solution that had been allowed to stand for 1.5-2 hours at room temperature, a saturated solution of sodium bicarbonate was added, the methanol was distilled off in vacuo over a period of 30 minutes and the o-nitroaniline formed was extracted with ether. The content of sodium nitrite in the aqueous alkaline solution, left after removal of o-nitroaniline, was determined. For this purpose the solution was evaporated on the water-bath until crystals of mineral salts began to separate, in order to remove residual ether and alcohol which interfere with the nitrite determination. Then to the solution was added a weighed quantity (about 0.0015 mole) of sulfamic acid and, with stirring, 70-100 ml of 10% sulfuric acid to a distinct acid reaction to Congo. The excess sulfamic acid was back-titrated with 0.1 N nitrite solution. The analytical data are shown in Table 3.

A solution of the triazene in 16.5% sodium methylate solution after standing at room temperature for 1.5-2 hours was treated with 20 ml of a saturated sodium bicarbonate solution and the methyl alcohol was distilled off in vacuo. The resulting solution was neutralized by mixing with 10% sulfuric acid to pH 8 and steam distilled. The distillate contained formaldehyde which was identified by the color reactions with phenylhydrazine and sodium nitroprusside [15] and with phenylhydrazine and potassium ferricyanide [16].

For the quantitative determination of formaldehyde in the triazene reaction products a sample of the triazene in sodium methylate was treated as described above and steam distilled. The distillate was collected below the surface of a solution of 15 ml of 0.1 N hydroxylamine hydrochloride in 35 ml of water until the total volume was 250 ml. The hydrochloric acid was back-titrated with 0.1 N sodium hydroxide potentiometrically, with a glass electrode, because coloration of the distillate by o-nitroaniline interfered with titration with an indicator. Control experiments showed that 96% of a known amount of formaldehyde can be found by the method described and that at pH 8 nitrous acid does not distill over from the solution which contains nitrite.

On titration of three samples of the triazene of 0.2250 g each, 5.5, 5.4 and 5.9 ml of 0.1 N alkali were required, corresponding to the formation of 54-59% of the formaldehyde theoretically possible for complete decomposition of the triazene.

Interaction of o-nitrophenyl-N-nitramine with sodium methylate solution. 0.001 mole of o-nitrophenyl-N-nitramine was dissolved in 20 ml of a 30% solution of sodium methylate in methanol. After 2 hours the solution was diluted with bicarbonate and extracted with ether. No trace of amine could be isolated from the ether. In another experiment the solution, after treatment with bicarbonate, was acidified to a positive reaction for mineral acid. No nitrous acid was found in the solution; only a trace of nitric acid was detected (by means of diphenylamine).

Behavior of N-nitrotriazenes in an acidic medium. a) Weighed quantities of the triazene were mixed with buffer solutions of pH from 1 to 7 and allowed to stand for 6 weeks. Each sample was then tested for nitric acid and amine.

For determination of nitric acid, sulfuric acid (about 60%) was added to a test portion, the solution was steam distilled and we tested for nitric and nitrous acids in the distillate. For determination of amine, the residue after distillation was neutralized with 10% alkali and extracted with ether. The ether was distilled from the extract and the residue was dissolved in concentrated hydrochloric acid and treated with nitrite. In none of the samples examined were even traces of either nitric acid or amine found.

b) A weighed sample of the triazene was heated in 68% sulfuric acid and the distillate was collected in water containing diphenylamine sulfate as an indicator for nitric acid. Nitric acid was not found in any of the test samples. The sulfuric acid solution from which the distillate was obtained was diluted with water and neutralized with strong alkali. The resulting solution was extracted with ether. The residue after removal of the ether from the extract, which was deep-yellow in color, was treated with acid and then with nitrite and added to a sodium carbonate solution of R-salt or β-naphthol. A coloration was obtained, indicating the presence of a small quantity of amine.

SUMMARY

1. It has been established that in contrast to methylaryltriazene-N-sulfonic acids that split off the sulfonic

group in acidic media, N-nitrosubstituted methylaryltriazenes under the same conditions do not split off the nitro group but decompose to a phenol, nitrogen, an alcohol and nitrous oxide. Such reaction courses are explained by the high polarity of the bond between nitrogen and sulfur in comparison with that between two nitrogens.

2. It is shown that methylaryl-N-nitrotriazenes have the properties of pseudo acids. They dissolve in alkalis and in basic solvents with a marked deepening in color. On allowing these methylaryl-N-nitrotriazene solutions to stand they decompose with the formation of the arylamine, nitrite, nitrogen and formaldehyde.

3. An explanation of the mechanism of the decomposition reaction of methylaryl-N-nitrotriazenes in alkaline media is put forward, according to which a proton begins to split off from the methyl group under the action of hydroxyl or methoxyl, with the formation of an unstable carbanion which is then converted to the N-methylene derivative of the aryltriazene by fission of the nitro group in the form of a nitrite anion.

4. It is shown that the proposed mechanism explains satisfactorily the reactions of various aliphatic N-nitro and C-nitro derivatives taking place in alkaline media, with elimination of the nitro group in the form of a nitrite anion and with intramolecular rearrangement of bonds, and that such reactions must be included in the known class of nucleophilic elimination reactions.

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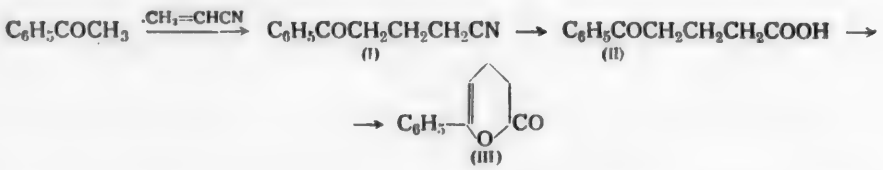
δ-LACTONES

XII. SYNTHESIS AND PROPERTIES OF 6-PHENYL-3,4-DIHYDRO-α-PYRONE

M. Iu. Lur'e, I. S. Trubnikov, N. P. Shusherina and R. Ia. Levina

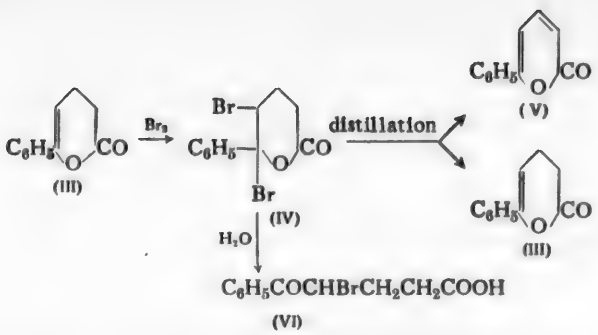
In our previous communications we described a method of synthesis of unsaturated δ-lactones (3,4-dihydro-α-pyrones) from monocyanoethylated aliphatic and alicyclic ketones [1-4]. In the present work the unsaturated δ-lactone, 6-phenyl-3,4-dihydro-α-pyrone (III), was prepared by this method from a monocyanoethylated aliphatic-aromatic ketone (acetophenone).



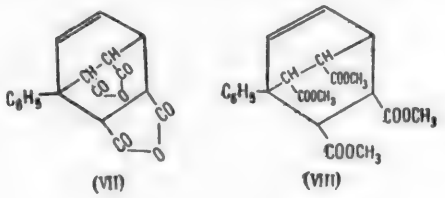
It is known from published data that cyanoethylation of acetophenone leads to the production of either the tricyanoethylated derivative [5], or of a mixture of monocyanoethylated (yield 13%) and dicyanoethylated acetophenone [6]. We have succeeded in finding conditions in which the cyanoethylation of acetophenone leads to the production of only the monocyanoethylated derivative, γ-benzoylbutyronitrile (I), in 28-35% yield. Hydrolysis of the nitrile (I) to γ-benzoylbutyric acid (II) and conversion of the latter to the lactone (III) took place with yields of 100 and 75% respectively.

Hydrolysis of the resulting unsaturated δ-lactone led to the formation of the original γ-benzoylbutyric acid, and alcoholysis and ammonolysis to the ester and amide respectively.

It was shown further that by the action of an equimolecular quantity of bromine on the lactone (III) a liquid dibromide (IV) is formed that fumes strongly in the air and, like the dibromolactones previously described by us [7, 8], is an extremely reactive compound. Thus the dibromolactone (IV) is converted on treatment with water to γ-bromo-γ-benzoylbutyric acid (VI) in 86.5% yield (as was shown by us previously [8] for other dibromolactones). On vacuum distillation in a current of dry air the dibromolactone is converted to 6-phenyl-α-pyrone (phenylcoumalin, V); however, simultaneously with phenylcoumalin (yield 14%) the original unsaturated δ-lactone (III) is formed. Thus, on distillation of the dibromolactone (IV), as well as elimination from it of two molecules of hydrogen bromide, which leads, as we have previously reported [7], to the formation of the α-pyrone (V), elimination of bromine with the formation of the original lactone also takes place.



The 6-phenylcoumalin (V) so obtained was characterized by the double maleic anhydride adduct (VII); by hydrolysis of the adduct and subsequent methylation the tetramethyl ester of the tetrabasic acid (VIII) was obtained.



EXPERIMENTAL

γ-Benzoylbutyronitrile (I). 48 g of acrylonitrile was added over a period of 3 hours, with vigorous stirring and water-cooling, to a mixture of 480 g of freshly redistilled* acetophenone and 2 ml of a saturated methanol solution of potassium hydroxide, at such a rate that the temperature did not exceed 25°. The reaction mixture was then stirred for a further 1-2 hours at room temperature and allowed to stand overnight; after the acetophenone was distilled off the residue was redistilled in vacuo. Monocyanoethylated acetophenone (I) was obtained in yields, in separate experiments, of 44 to 55 g, i.e., 28-35%.

B. p. 172-175° at 7-8 mm. Literature data: b. p. 178-182° at 8 mm, m. p. 38-39° (from alcohol) [6]; b. p. 125° at 1 mm, $n^{20}D$ 1.5326 [9].

Semicarbazone, m. p. 175° (from aqueous alcohol). Literature data [10]: m. p. 176-177° (from chloroform).

Found %: N 24.47, 24.26. $C_{12}H_{14}ON_4$. Calculated %: N 24.33.

γ-Benzoylbutyric acid (II). A mixture of 44 g of the nitrile and 240 ml of dilute (2:1) hydrochloric acid was refluxed for 3 hours. The crystals which separated on cooling (with shaking) were filtered off and dried (yield, quantitative). M. p. 125-126° (from water). Literature data: m. p. 126-127° [11].

6-Phenyl-3,4-dihydro-α-pyrone (III). A mixture of 25 g of γ-benzoylbutyric acid and 150 ml of acetic anhydride was refluxed for 5 hours, the acetic anhydride distilled off and the residue redistilled in vacuo. 6-Phenyl-3,4-dihydro-α-pyrone distilled at 174-175° (10 mm) and melted at 43-45° (from benzene or petroleum ether). Yield 17 g (75%). This compound is not described in the literature.

Found %: C 75.60, 75.42; H 5.88, 5.90. $C_{11}H_{10}O_2$. Calculated %: C 75.84; H 5.79.

The lactone obtained was easily hydrolyzed on heating with dilute alkalis, being converted to the original γ-benzoylbutyric acid (m. p. 125-126°).

* Acetophenone that has been kept for a long time cyanoethylates with poorer yields or does not react at all.

Alcoholysis of the lactone (III). A solution of 12 g of the lactone in 60 ml of anhydrous alcohol was saturated with hydrogen chloride while cooling in ice water. After the usual treatment of the reaction mixture, 11.5 g (76%) of ethyl γ-benzoylbutyrate was obtained.

B. p. 178-180° (10 mm), m. p. 23-25°, $n^{20}D$ 1.5110. Literature data [12]: b. p. 315°.

Found %: C 71.29, 71.11; H 7.30, 7.33. $C_{13}H_{16}O_3$. Calculated %: C 70.86; H 7.31.

2,4-Dinitrophenylhydrazone, m. p. 126-127° (from ethyl alcohol).

Found %: C 57.26, 57.27; H 5.29, 5.13. $C_{19}H_{20}O_6N_4$. Calculated %: C 56.98; H 5.04.

Ammonolysis of lactone (III). On shaking the lactone with concentrated aqueous ammonia, γ-benzoylbutyramide was obtained in 90% yield; m. p. 144° (from water). Literature data [10]: m. p. 144°.

Bromination of lactone (III). An equimolecular quantity of bromine was added to the lactone (III) in absolute ether, with cooling (in the absence of atmospheric moisture). The ether was evaporated in a current of dry air and the liquid dibromide (IV) which fumes in air, was redistilled in vacuo or reacted with water.

Vacuum distillation of the dibromolactone (IV). The liquid dibromide (IV), obtained from the bromination of 13 g of the lactone with an equimolecular quantity of bromine was heated for 0.5 hours (up to distillation temperature) in a current of dry air in vacuo (8 mm) and then slowly distilled. The distillate (6.5 g; b. p. 173-185° at 8 mm) was treated in the cold with 2 N sodium hydroxide for hydrolysis of the lactone (III)* to γ-benzoylbutyric acid. The material that was not soluble in alkali and which crystallized with difficulty on cooling (1.8 g: yield 14% calculated on the initial unsaturated lactone) consisted of 6-phenylcoumalin (V). M. p. 67.5° (from petroleum ether). Literature data [13]: m. p. 68°.

On acidification of the alkaline solution, γ-benzoylbutyric acid (4.7 g) was isolated. M. p. 125-126° (from water).

Isolation of 6-phenylcoumalin from the mixture containing the unsaturated δ-lactone (III) was also possible by prolonged boiling of the mixture with water because 6-phenylcoumalin is insoluble in water and does not react with it, and the unsaturated δ-lactone is hydrolyzed to γ-benzoylbutyric acid.

Maleic anhydride adduct of 6-phenylcoumalin. A mixture of 0.7 g (0.004 mole) of the pyrone (V) and 0.8 g (0.008 mole) of maleic anhydride in 4 ml of dry xylene was refluxed for 20 hours. 1.2 g (80%) of the double adduct (VII) was obtained. This compound is not described in the literature. M. p. 296-297° (from anhydrous acetone).

Found %: C 66.72, 66.82; H 3.88, 3.82. $C_{18}H_{12}O_6$. Calculated %: C 66.64; H 3.72.

On dissolving the adduct in 10% sodium hydroxide solution and subsequent acidification with hydrochloric acid a crystalline acid was obtained which titrated as tetrabasic; on treating a solution of this in ether with an ethereal solution of diazomethane the tetramethyl ester of (VII) was obtained. M. p. 191-192° (from aqueous alcohol).

Found %: C 63.19, 63.10; H 5.91, 6.09. $C_{22}H_{24}O_8$. Calculated %: C 63.48; H 5.80.

γ-Bromo-γ-benzoylbutyric acid. The dibromide (IV) obtained from 13 g of the lactone was treated with cold water, with mechanical stirring. The crystals of γ-bromo-γ-benzoylbutyric acid that separated were filtered off and dried. Yield 17.5 g (86.5%). M. p. 96-97° (from CCl_4). Literature data [14]: m. p. 97-98°. A mixed melting point with a sample of the same acid prepared by direct bromination of γ-benzoylbutyric acid was not depressed.

Found %: C 49.07, 49.09; H 4.18, 4.10. $C_{11}H_{11}O_3Br$. Calculated %: C 48.72; H 4.09.

SUMMARY

1. A method has been developed for the preparation of monocyanoethylated acetophenone (γ-benzoylbutyronitrile) in yields of 28-35%.

* The lactone (III) could be isolated by careful fractional distillation of the distillate (in a current of dry air). B. p. 174-176° (10 mm), m. p. 40-41° (from benzene).

2. By hydrolysis of γ-benzoylbutyronitrile to γ-benzoylbutyric acid and subsequent heating with acetic anhydride the unsaturated δ-lactone, 6-phenyl-3,4-dihydro-α-pyrone, not previously described in the literature, was obtained (in 75% yield).

3. From the dibromide of 6-phenyl-3,4-dihydro-α-pyrone, 6-phenylcoumalin was obtained (yield 14%) by distillation, and on treatment with water, it gave γ-benzoylbutyric acid (yield 86.5%).

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PREPARATION OF OXIDES OF α,β-UNSATURATED HIGHER FATTY ACIDS AND STUDY OF THEIR PROPERTIES

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The first researches on the preparation of the oxide of elaidic acid and study of its properties were carried out by A. A. Al'bitskii [1]. It was first observed by G. V. Pigulevskii that on oxidation of oleic, linoleic and linolenic acids with Prilezhaev's reagent, oxygenated derivatives were obtained, i.e., oxides [2-4]. Subsequently a number of investigators have been concerned with the preparation of oxides of unsaturated higher fatty acids [5-12].

It is known that the oxides of unsaturated higher fatty acids are highly reactive. The most characteristic reaction is their interaction with water with the formation of dihydroxy acids [3,6,9,13,14].

The oxides can also be hydrogenated. The addition of hydrogen to oxides is of great interest since it brings about the possibility of conversion of unsaturated fatty acids, from which the oxides are readily prepared, to hydroxy fatty acids. This enabled G. V. Pigulevskii and Z. Ia. Rubashko [15, 16], who were the first to investigate the catalytic hydrogenation of the oxides of oleic and erucic acids, to put forward a new method of preparation of hydroxy acids.

We were interested to prepare oxides of unsaturated fatty acids with the oxide ring in the position adjacent to the carboxyl group and to study their properties, since there is no information on such oxides in the literature. For the solution of this problem we oxidized the trans-isomers of the following fatty acids with benzoyl hydroperoxide (perbenzoic acid): hexadecen-2-acid-1 (2-hexadecanoic acid), octadecen-2-acid-1 (2-octadecanoic acid) and docosen-2-acid-1 (2-docosanoic acid).

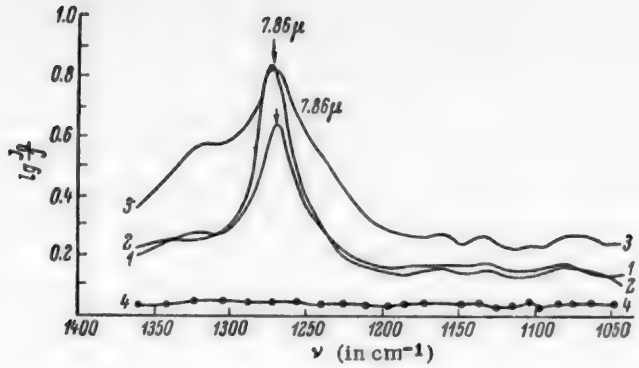
Our investigations showed that the free acids react very slowly with benzoyl hydroperoxide (perbenzoic acid). In view of this we decided to oxidize the methyl esters of the acids. This enabled the oxidation process to be accelerated considerably and the oxides of the acids mentioned to be obtained in satisfactory yields (Table 2).

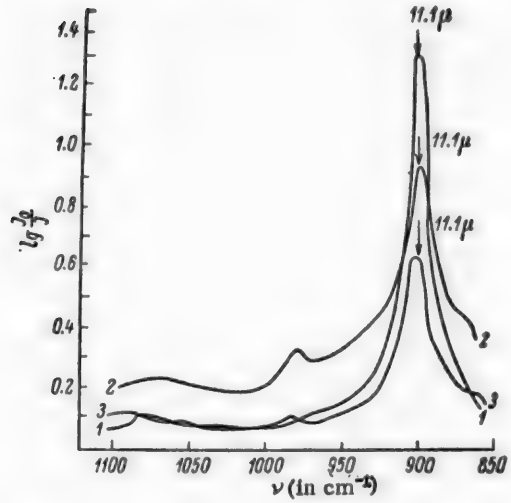
In order to study the chemical properties of the oxides obtained the latter were hydrated and hydrogenated.

It was found that the oxides prepared by us are readily hydrated on boiling with distilled water, acidified with a few drops of sulfuric acid. As a result of the hydration of the oxides investigated 2,3-dihydroxyhexadecanoic acid, 2,3-dihydroxyoctadecanoic and 2,3-dihydroxydocosanoic acids were obtained and characterized (Table 3).

On hydrogenation of the oxides investigated by us in ethyl alcohol in the presence of platinum black as catalyst, the monohydroxy acids were obtained, and on opening of the oxide ring the hydroxyl group evidently takes up the position furthest from the carboxyl groupsince the hydrogenation products that we obtained, according to their properties, corresponded to 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids (Table 4). Their melting points are considerably lower than the corresponding 2-hydroxy acids. Mixed melting points with the 2-hydroxy acids gave a depression but with 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids there was no depression.*

* 2-Hydroxyhexadecanoic, 2-hydroxyoctadecanoic and 2-hydroxydocosanoic acids, required for comparison, were prepared by the method of Ponzio [17] and Le Sueur [18], and 3-hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids were prepared by the method of Eckert and Haller [19].





Infrared absorption spectra. 1) Hexadecen-2-acid-1 (trans) oxide (trans-2,3-epoxyhexadecanoic acid), 2) octadecen-2-acid-1 (trans) oxide (trans-2,3-epoxyoctadecanoic acid), 3) docosen-2-acid-1 (trans) oxide (trans-2,3-epoxydocosanoic acid).

In order to determine the position of the hydroxyl groups in the hydroxy acids obtained, the latter were oxidized with chromic acid in glacial acetic acid. From this oxidation keto acids were obtained with properties in close agreement with those of 3-ketohexadecanoic, 3-ketooctadecanoic and 3-ketodecosanoic acids (Table 5).

Hence, on hydrogenation of these oxides, opening of the oxide ring in fact takes place on the side nearest to the carboxyl group. This agrees with statements in the literature [10,15,16].

For complete characterization of the oxides investigated their absorption spectra in the infrared region were recorded (see Figures). It was found that in the spectra of the oxides in question there are intense, clearly defined, absorption bands with maxima at 11.1μ (about 900 cm^{-1}) and 7.86μ (about 1275 cm^{-1}), a little displaced toward the shorter-wave side of the spectrum resulting from the conjugation of the oxide ring with the C=O group of the carboxyl, since according to the literature [20, 21] these absorption maxima for the oxide of elaidic acid, where the oxide ring occurs between carbon atoms 9 and 10 (i.e., in the center of the molecule), are at 11.2μ (893 cm^{-1}) and 8.0μ (1250 cm^{-1}).

EXPERIMENTAL

1. Preparation of the Oxides of Hexadecen-2-Acid-1 (Trans) (Trans-2,3-Epoxy Hexadecanoic Acid), Octadecen-2-Acid-1 (Trans) (Trans-2,3-Epoxyoctadecanoic Acid), and Docosen-2-Acid-1 (Trans) (Trans-2,3-Epoxydocosanoic Acid)

a) Esterification of the acids. The acids were esterified with anhydrous methanol in the presence of sulfuric acid by the following method. To 25 g of the fatty acid was added 125 ml of methyl alcohol containing 9 g of sulfuric acid (d 1.84), and the mixture was heated on the water-bath for 1 hour with continuous mechanical stirring with a glass stirrer. The methyl esters of the fatty acids were isolated by diluting the reaction mixture with water and extracting with ether. The ether extract was washed with water to neutral reaction, dried and the ether distilled off. The ethers obtained after redistillation in vacuo had the following properties (Table 1).

TABLE 1

Name of ester and its structural formula	Melting point	Saponification equivalent
Methyl ester of hexadecen-2-acid-1 (trans) $CH_3(CH_2)_{12}-C(=H)-C(-H)-COOCH_3$	26.5°	208.84
Methyl ester of octadecen-2-acid-1 (trans) $CH_3(CH_2)_{14}-C(=H)-C(-H)-COOCH_3$	36.0	188.20
Methyl ester of docosen-2-acid-1 (trans) $CH_3(CH_2)_{18}-C(=H)-C(-H)-COOCH_3$	48.0	158.82

TABLE 2

Name of oxide and its structural formula	M.p.	Neutralization equivalent		Elementary analysis % C		Elementary analysis % H	
		found	calc.	found	calc.	found	calc.
Oxide of hexadecen-2-acid-1 (trans) $CH_3(CH_2)_{12}-C(-H)-C(-O-)-C(-H)-COOH$	78.5°	206.84	207.63	70.85	71.04	11.24	11.18
Oxide of octadecen-2-acid-1 (trans) $CH_3(CH_2)_{14}-C(-H)-C(-O-)-C(-H)-COOH$	83.5	187.87	188.10	72.35	72.41	11.80	11.48
Oxide of docosen-2-acid-1 (trans) $CH_3(CH_2)_{18}-C(-H)-C(-O-)-C(-H)-COOH$	89.5	158.91	158.35	74.50	74.50	12.01	11.94

TABLE 3

Name of dihydroxy acid	Melting point	Neutralization equivalent		Elementary analysis				Number of OH-groups found (Zerewitinoff method)
				% C		% H		
		found	calc.	found	calc.	found	calc.	
2,3-Dihydroxyhexadecanoic acid	116.5°	195.35	194.04	66.57	66.66	11.18	11.19	2.79
2,3-Dihydroxyoctadecanoic acid	126.5*	177.5	174.40	–	–	–	–	2.91
2,3-Dihydroxydocosanoic acid	130.0	150.0	150.69	70.94	70.90	12.08	11.91	2.98

* According to the literature [18], m. p. 126°.

TABLE 4

Hydroxy acid	Melting point	Neutralization equivalent		Elementary analysis				Number of OH groups found (Norman method)
				% C		% H		
		found	calc.	found	calc.	found	calc.	
3-Hydroxyhexadecanoic acid	84.5°	205.68	206.09	70.29	70.52	12.06	11.84	0.96
3-Hydroxyoctadecanoic acid	88.0*	186.30	186.85	–	–	–	–	1.01
3-Hydroxydocosanoic acid	92.5	158.17	157.44	73.93	74.08	12.39	12.45	1.0

* According to the literature [18], m. p. 89°.

TABLE 5

Keto acid	Melting point	Elementary analysis			
		% C		% H	
		found	calc.	found	calc.
3-Ketohexadecanoic	94.0°	70.86	71.04	11.10	11.18
3-Ketooctadecanoic	98.2*	–	–	–	–
3-Ketodocosanoic	105.0	74.58	74.50	11.84	11.94

* According to the literature [22], m. p. 99°.

(b) Oxidation of the methyl esters with benzoyl hydroperoxide (perbenzoic acid). To 5 g of the methyl ester of the unsaturated acid an ethereal solution of benzoyl hydroperoxide (perbenzoic acid) (0.01158 g of active oxygen in 1 ml of solution) was added in an amount corresponding to 100% excess over the quantity of active oxygen theoretically required. The mixture was heated on the water-bath to 30-40° in 2 hours, after which it was allowed to stand overnight at room temperature. A large quantity of hot water was then added and the oxide of the fatty acid ester which formed an upper layer was extracted with ether after cooling. The ethereal solution was washed twice with water, dried and filtered and the ether was distilled off. The oxide of the methyl ester obtained was saponified with alcoholic alkali and the soap obtained, after removal of the alcohol, was

treated with 20% sulfuric acid solution. The fatty acid oxide which separated was extracted with ether. The ethereal solution was washed with water to neutral reaction, dried and filtered. After removal of ether the oxide obtained was reduced to a fine powder in a porcelain dish, washed with a ten-fold quantity of petroleum ether to remove impurities, and filtered through an ordinary filter-paper. The analysis of the oxides made by this method is given in Table 2.

The yield of oxide varied between the limits 40-50%. In outward appearance they consist of white, fine-crystalline powder, readily soluble in ethyl ether, chloroform, acetone and alcohol. In petroleum ether they dissolve only on slight warming.

2. Study of the Chemical Properties of the Oxides

a) Hydration of the oxides. To 1.0 g of the oxide, 100 ml of distilled water acidified with 3-5 drops of conc. H_2SO_4, was added and the mixture was refluxed for 1-1.5 hours. On cooling the dihydroxy acid separated at the surface of the liquid in the form of white flakes. In order to separate it from the acid solution, the mixture was filtered through an ordinary filter-paper. The residue on the filter was washed to neutral reaction and dried, first between sheets of filter-paper and then in the air, and recrystallized twice from chloroform. The yield of dihydroxy acid varied between the limits of 85-95%. The results of examination of the dihydroxy acids obtained are given in Table 3.

b) Hydrogenation of the oxides. 10 ml of a 0.330 M alcoholic solution of the oxide was placed in each of two glass vessels ("ducks"), which were fixed on a shaker and connected to two burettes filled with electrolytic hydrogen. After the systems had been swept through with hydrogen the catalyst was introduced (0.09 g of platinum black) and shaking begun. The hydrogen absorbed at definite intervals was calculated. The volume of hydrogen absorbed was brought to 0° and 760 mm. On hydrogenation of the oxide of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), 82.9 ml of hydrogen was absorbed, the oxide of octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid oxide) – 74.9 ml of hydrogen and the oxide of docosen-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) – 62.9 ml (the calculated quantities of H_2 are 82.9, 75.0 and 63.2 ml respectively). The hydrogenation products of the oxides are fine-crystalline, white powders with high melting points and are evidently 3-monohydroxy acids. The results of analysis of the hydroxy acids obtained are given in Table 4.

Proof of the position of the hydroxyl groups in the 3-monohydroxy acids obtained. To 3 g of the hydroxy acid dissolved in 30 ml of glacial acetic acid 35 ml of an acetic acid solution, containing the theoretically required quantity of chromic anhydride, was added gradually with shaking over a period of 30 minutes. The reaction mixture was allowed to stand overnight. It was then heated on the water-bath for 10 minutes. On cooling and diluting with water a fine-crystalline precipitate separated which was filtered off and washed with water. After two recrystallizations from ethyl alcohol the keto acids obtained had constant melting points (Table 5).

SUMMARY

1. The oxides of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid) and docosen-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) have been synthesized for the first time and the properties of these oxides have been studied.

2. It was found that the oxides obtained are easily hydrated to form dihydroxy acids. 2,3-Dihydroxyhexadecanoic, 2,3-dihydroxyoctadecanoic and 2,3-dihydroxydocosanoic acids were obtained, of which the first and third are not described in the literature.

3. On hydrogenation the oxides form hydroxy acids. The opening of the oxide ring is such as to place the hydroxyl group on the carbon atom furthest away from the carboxyl group. 3-Hydroxyhexadecanoic, 3-hydroxyoctadecanoic and 3-hydroxydocosanoic acids were obtained, of which the first and last are not described in the literature.

4. The infrared absorption spectra of the oxides of hexadecen-2-acid-1 (trans) (trans-2,3-epoxyhexadecanoic acid), octadecen-2-acid-1 (trans) (trans-2,3-epoxyoctadecanoic acid) and docosan-2-acid-1 (trans) (trans-2,3-epoxydocosanoic acid) have been recorded.

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SUBSTANCES CAPABLE OF COMPLEX FORMATION

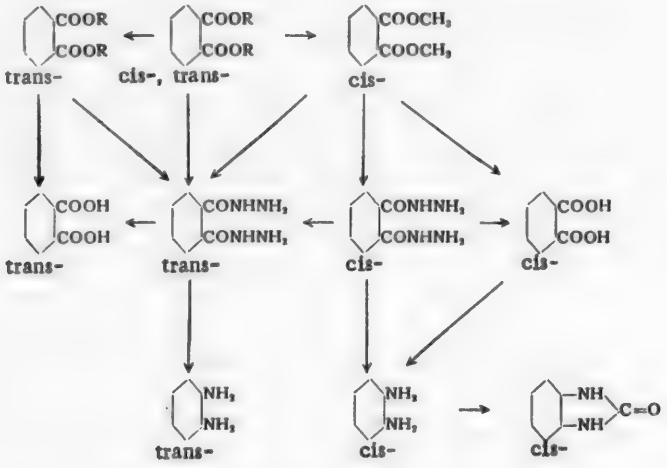
III. CIS-1,2-DIAMINOCYCLOHEXANE

V. G. Iashunskii

It has been shown earlier [1] that "Complexon-IV" is trans-1,2-diaminocyclohexane-N,N'-tetraacetic acid, and it is obtained by the condensation of trans-1,2-diaminocyclohexane with monochloroacetic acid. It seemed of interest to synthesize the cis-isomer of this Complexon.

Until recently, however, there has been no mention in the literature of cis-1,2-diaminocyclohexane from which this Complexon could be obtained. At the time of completion of the present work a short communication [2] appeared, in which mention was made of the preparation of cis-1,2-diaminocyclohexane by degradation of cis-hexahydrobenzimidazolone.

The present communication describes the synthesis of cis-1,2-diaminocyclohexane by means of the Curtius reaction (by a scheme analogous to that for the preparation of the trans-isomer of this diamine [1]), and the Schmidt reaction.



In conformity with the data in the literature [4] the product of hydrogenation of diethyl (or dimethyl) phthalate over Raney nickel, from which we have previously prepared the dihydrazide of cis-1,2-cyclohexanedicarboxylic acid and subsequently by a Curtius degradation, trans-1,2-diaminocyclohexane, is a mixture of cis- and trans-1,2-cyclohexanedicarboxylic acids. Hence, in one of these stages (preparation of the dihydrazide or the Curtius reaction) cis-trans isomerization takes place. We succeeded in showing that this isomerization takes place on boiling the esters with hydrazine hydrate, and the dihydrazide formed, with m. p. 229-231°, has the trans-configuration. On hydrolysis it yielded trans-1,2-cyclohexanedicarboxylic acid. The configuration of the dihydrazide obtained was confirmed also by comparing it with a sample of the dihydrazide prepared by the interaction of diethyl trans-1,2-cyclohexanedicarboxylate with hydrazine hydrate.

Dimethyl cis-1,2-cyclohexanedicarboxylate under the same conditions, and also on carrying out the reaction in alcoholic solution at 120° in a sealed ampoule, is converted entirely to the trans-dihydrazide.

An example of a similar rearrangement is described in the literature [5]: under analogous conditions the corresponding trans-dihydrazide was obtained from the diester of cis-3,4-thiophanedicarboxylic acid.

cis-1,2-Cyclohexanedicarboxylic acid dihydrazide of m. p. 123-124.5° was prepared by reacting dimethyl cis-1,2-cyclohexanedicarboxylate with hydrazine hydrate in methyl alcohol at room temperature. Hydrolysis of this hydrazide with hydrochloric acid gave cis-1,2-cyclohexanedicarboxylic acid. On heating the cis-dihydrazide above its melting point it solidifies and melts again at 228.5-229.5°, i.e., it isomerizes to the trans-dihydrazide.

The cis-dihydrazide was subjected to the Curtius degradation whereby, without isolation of the intermediate diazine and diurethane, the diamine was obtained successfully, the dihydrochloride, dibenzoyl, diacetyl and dibenzenesulfonyl derivatives of which differed from the corresponding derivatives of the trans-diamine, giving mixed melting point depressions. On reacting with phosgene, cis-hexahydrobenzimidazolone was isolated. All this provides an adequate basis for considering that the diamine obtained has the cis-configuration. Thus, our results confirm the statement in the literature [6] that cis-trans isomerization does not occur in the Curtius reaction.

We also synthesized cis-1,2-diaminocyclohexane directly from cis-1,2-cyclohexanedicarboxylic acid by the Schmidt reaction. Here, as in the Curtius rearrangement, the configuration of the original compound is preserved. The reaction was carried out in two ways: a) by treating the cis-acid with a chloroform solution of hydrazoic acid in the presence of conc. H_2SO_4 and b) by adding dry sodium azide to a mixture of a benzene solution of the cis-acid and conc. H_2SO_4. In both cases, after steam distilling the base, cis-1,2-diaminocyclohexane dihydrochloride was obtained.

EXPERIMENTAL

Diethyl trans-1,2-cyclohexanedicarboxylate (b. p. 127-128° at 7 mm, $n^{25}D$ 1.4482) and diethyl cis-1,2-cyclohexanedicarboxylate (b. p. 136-137.5° at 10 mm, $n^{25}D$ 1.4500) were obtained from the product of hydrogenation of diethyl phthalate over Raney nickel [4]. The dimethyl ester of the cis-acid was prepared by the same method and also from the butadiene-maleic anhydride adduct [7].

Reaction of the 1,2-cyclohexanedicarboxylic esters with hydrazine hydrate. 11.4 g of diethyl trans-1,2-cyclohexanedicarboxylate was added over a period of 1 hour to 12.5 g of 100% hydrazine hydrate at its boiling point. The mixture was heated a further 16 hours at 130° to form a solid, white mass, which was soluble in hot water. The liquid was separated from the crystals that separated on cooling and after recrystallizing from water, 8.2 g of trans-1,2-cyclohexanedicarboxylic acid dihydrazide, with m. p. 229-231° (with rapid heating of the capillary tube), was obtained.

Diethyl cis-1,2-cyclohexanedicarboxylate gave with hydrazine hydrate under the same conditions, a dihydrazide with m. p. 227.5-228.5°. A mixed melting point with the trans-dihydrazide gave no depression. Small quantities of the trans-dihydrazide and of the original ester were isolated from the mother liquor. Similar results were obtained with the dimethyl ester.

A mixture of 5 g of the cis-dimethyl ester, 5 g of hydrazine hydrate and 5 ml of absolute methyl alcohol were heated in a sealed tube at 115-120° for 4 hours. Only the trans-dihydrazide of m. p. 229-230.5° was obtained on working up the reaction mixture. On heating the trans-dihydrazide with concentrated hydrochloric acid, trans-1,2-cyclohexanedicarboxylic acid of m. p. 219.5-220.5° (from 25% aqueous acetone) was obtained.

cis-1,2-Cyclohexanedicarboxylic acid dihydrazide. A mixture of 30 g of dimethyl cis-1,2-cyclohexanedicarboxylate, 37.5 g of hydrazine hydrate and 50 ml of methyl alcohol was left to stand for a week at room temperature. The reaction mixture was then evaporated in vacuo (water-pump) at a temperature not above 50°. The residue was pressed out on a filter and washed with methyl alcohol and ether. After a two-fold recrystallization from absolute ethyl alcohol 18.85 g of the cis-dihydrazide, of m. p. 123-124.5°, was obtained.

Found %: N 27.91. $C_8H_{16}O_2N_4$. Calculated %: N 27.98.

On heating with concentrated hydrochloric acid this hydrazide gave cis-1,2-cyclohexanedicarboxylic acid of m. p. 189.5-190.5° (from water).

A small quantity of the cis-dihydrazide was heated above its melting point: at about 130° the material solidified and melted again at 215-220°. After recrystallizing from water it had m. p. 227.5-229.5°. A mixed melting point with the trans-dihydrazide gave no depression.

cis-1,2-Diaminocyclohexane. 7.5 g of the cis-dihydrazide was added with stirring and cooling to 26 ml of 10% hydrochloric acid. 30 ml of ether was then added and a solution of 5.32 g of sodium nitrite in 12 ml of water was added gradually at such a rate that the temperature of the mixture remained within the limits of 18 to 20°. After stirring at this temperature for 10 minutes the upper layer was separated off and the aqueous layer was extracted twice with 20 ml of ether. The combined ethereal extracts were dried for a short time over fused calcium chloride, filtered and mixed with 40 ml of absolute ether. The ether was slowly distilled from the resulting solution at 65-70° (in steam). The residue was refluxed for 1 hour, 36 g of potassium hydroxide and 100 ml of methyl alcohol were added and refluxing was continued for a further 2 hours on an oil bath at 120-130°. The reaction mixture was distilled with superheated steam. The distillate was acidified with hydrochloric acid (about 14 ml of 10% HCl) and evaporated to dryness on the water bath, yielding 4.2 g of crude cis-1,2-diaminocyclohexane dihydrochloride.

100 ml of a freshly prepared 2 N solution of hydrazoic acid in chloroform was added to a mixture of 13.5 g of cis-1,2-cyclohexanedicarboxylic acid, of m. p. 189-190.5°, prepared by saponification of the dimethyl ester, and 26 ml of conc. H_2SO_4 at 40°, with stirring. Stirring was continued at this temperature for 16 hours, after which the mixture was poured onto ice and the aqueous layer was steam distilled after being made alkaline. After evaporation of the acidified distillate, 3.5 g of the cis-diamine dihydrochloride was obtained.

6.5 g of sodium azide was added in small portions over a period of 1 hour to a mixture of 6 g of the cis-acid, 14 ml of conc. H_2SO_4 and 50 ml of chloroform at 40°; after stirring at this temperature for 10 hours the reaction mixture was treated as described above and 1.2 g of the cis-diamine dihydrochloride was obtained. The free base was isolated by ether extraction after treatment of a concentrated aqueous solution of cis-1,2-diaminocyclohexane dihydrochloride with solid alkali. It was redistilled at 92-93° and 18 mm.

cis-1,2-Diaminocyclohexane dihydrochloride was prepared by treatment of the base with alcoholic hydrogen chloride solution. M. p. 307-310°.

Found %: C 38.44; H 8.72; Cl 37.79. $C_6H_{14}N_2 \cdot 2HCl$. Calculated %: C 38.52; H 8.62; Cl 37.91.

The remaining derivatives were prepared both from the free base and from the unpurified dihydrochloride isolated directly from the Curtius and Schmidt reactions.

Dibenzoyl derivative (Schotten-Baumann method), m. p. 186.5-187° (from alcohol).

Found %: C 74.45; H 6.92; N 8.72. $C_{20}H_{22}O_2N_2$. Calculated %: C 74.50; H 6.88; N 8.69.

Diacetyl derivative – an oily product.

Dibenzenesulfonate, m. p. 165-166° (from 40% alcohol).

Found %: N 7.09. $C_{18}H_{22}O_4N_2S_2$. Calculated %: N 7.10.

Dipicrate, m. p. 260° (decomp., from water).

Found %: N 19.27. $C_6H_{14}N_2 \cdot 2C_6H_3O_7N_3$. Calculated %: N 19.71.

In the communication [2] mentioned above the following constants for cis-1,2-diaminocyclohexane are given: free base, b. p. 93-95° at 20 mm; dihydrochloride, m. p. about 270°; dibenzoyl derivative, m. p. 184-185°; dipicrate, m. p. 160° (decomp.).

cis-Hexahydrobenzimidazolone. 0.9 g of cis-1,2-diaminocyclohexane in 8 ml of 10% potassium hydroxide solution was treated, with vigorous cooling, with 8 ml of an 16% toluene solution of phosgene. The reaction mixture was evaporated to dryness and the residue was extracted with hot benzene. After removal of the benzene a white powder remained, which after recrystallizing from acetone had m. p. 147-148°. According to the literature: m. p. 147-149° [3].

SUMMARY

1. It has been established that by reacting hydrazine hydrate with esters of cis-and trans-1,2-cyclohexanedicarboxylic acid, by heating to 120-130°, only trans-1,2-cyclohexanedicarboxylic acid dihydrazide is obtained. The cis-dihydrazide is obtained by carrying out the reaction at room temperature.

2. cis-1,2-Diaminocyclohexane, which was characterized by a number of derivatives, was synthesized by the Curtius reaction from cis-1,2-cyclohexanedicarboxylic acid dihydrazide. The cis-diamine was prepared also by the Schmidt reaction from cis-1,2-cyclohexanedicarboxylic acid.

3. The statement in the literature that cis-trans isomerization does not occur in the preparation of amines by the Curtius and Schmidt reactions has been confirmed.

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RESEARCH IN THE FIELD OF SUBSTITUTED PHENYLOSAZONES AND PHENYLHYDRAZONES

II. SOME NEW NITROPHENYLOSAZONES OF DIHYDROXYTARTARIC ACID

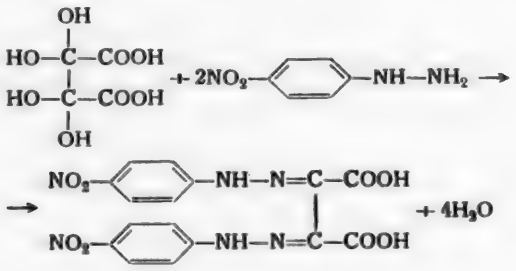
N. V. Chugreeva

It is evident from numerous sources in the literature that phenylosazones and phenylhydrazones (as well as their nitro and halogen derivatives) of compounds containing carbonyl groups have been prepared and used only for the identification of these compounds up to the present time. For this purpose such characteristics as melting point, crystalline form, color, and solubility in organic compounds are most often used.

In a number of papers describing the methods of preparation and properties of some nitrophenylhydrazones and nitrophenylosazones it is pointed out that the latter are capable of dissolving in alkali with a change in color, thus displaying indicator properties to some degree [1-6].

These facts led us* to synthesize and examine not only the phenylhydrazones and osazones already described in the literature but also a number of other compounds, the properties of which were not known. This paper is concerned with some dihydroxytartaric acid nitrophenylosazones, the structure of which suggests that they are capable of indicator action.

There are a number of methods for synthesizing nitrophenylosazones and nitrophenylhydrazones. For our purpose we utilized the direct reaction of the carbonyl-containing compounds with nitro derivatives of phenylhydrazine, which proceeds (in the case of dihydroxytartaric acid and p-nitrophenylhydrazine) according to the following scheme:



EXPERIMENTAL

Dihydroxytartaric acid p-nitrophenylosazone. For the preparation of this osazone we did not actually start with the relatively unstable hydrate of dihydroxytartaric acid but with its disodium salt, using the method described by Kul'berg [7] for unsubstituted phenylosazones, with the introduction of slight modifications to the method. With the object of improving the purity of the product without decreasing its yield, we filtered the precipitate using a Büchner funnel attached to an aspirator and washed (at least 6 times) with small portions of distilled water slightly acidified with hydrochloric acid; this procedure was followed by at least the same number of washings with cooled aqueous (50%) alcohol solution (instead of washing with acetone as recommended previously).

* This work was carried out under the guidance of Professor L. M. Kul'berg.

Found %: N 20.11, 20.21. $C_{16}H_{12}O_8N_6$. Calculated %: N 20.18.

Dihydroxytartaric acid p-nitrophenylosazone is a red, crystalline substance (with a slight brownish tinge), melting with decomposition at 234.5-235° (from alcohol). It is practically insoluble in cold and only slightly soluble in hot water, benzene, chloroform and carbon tetrachloride; it dissolves rather more readily in ethyl alcohol and acetone and is quite soluble in methyl alcohol. Saturated aqueous solutions are pale yellow in color, and alcoholic solutions are yellow-orange. The color of the chloroform solution is close to that of an alcoholic solution of the same concentration. Solutions in benzene and carbon tetrachloride are pale orange with a pink tinge.

When added to a solution of sodium or potassium hydroxide (0.5N or above), crystalline dihydroxytartaric acid p-nitrophenylosazone dissolves readily and gives a blue color, showing that this osazone has indicator properties. Solutions of the osazone in water and in organic solvents behave in the same way, i.e., they turn blue or dark blue when they are added to alkaline solutions of the stated concentrations. The aqueous and alcoholic solutions are unstable and lose their indicator properties comparatively rapidly (storage period not more than 3 days). Solutions in other organic solvents (benzene, toluene, chloroform, carbon tetrachloride) are considerably more stable and can be kept for weeks or even months without loss of indicator properties. Dry dihydroxytartaric acid p-nitrophenylosazone is completely stable; samples of it tested immediately after preparation and 2 years after preparation are absolutely identical in properties.

By careful addition of concentrated (25%) ammonia solution to the crystalline p-nitrophenylosazone and subsequent removal of water and excess ammonia by heating on a boiling water bath, we obtained a reddish-brown substance – the ammonium salt of dihydroxytartaric acid p-nitrophenylosazone. An advantage of this salt over the corresponding osazone of the free acid is its better solubility in water at ordinary temperatures, which enables us to dispense with the use of alcohol in practical applications.

Dihydroxytartaric acid 2,4-dinitrophenylosazone. The synthesis of this substance was achieved by the scheme described above for dihydroxytartaric acid p-nitrophenylosazone. The 2,4-dinitrophenylosazone is rather more soluble in alcohol than the p-nitrophenylosazone, consequently the precipitate was washed initially with cooled distilled water (not less than 7-8 times, small portions) and finally (3-4 times) with cold aqueous ethyl alcohol (40%). The washed precipitate was pressed between sheets of filter paper, after which it was immediately transferred to an oven and dried at 105-110° to constant weight.

The ammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone can be prepared easily by direct interaction of the crystalline osazone with concentrated ammonia solution. After the excess ammonia was evaporated off on a boiling water bath, a bright red crystalline product with a slight orange tinge remained. After it was dried to constant weight at 120-125°, the ammonium salt was unchanged in properties. M. p. 311-311.5° (decomp.). Analysis for nitrogen content showed that the product was the monoammonium salt.

Found %: N 24.38. $C_{16}H_{13}O_{12}N_9$ (acid salt). Calculated %: N 24.09. $C_{16}H_{16}O_{12}N_{10}$ (neutral salt). Calculated %: N 25.92.

The 2,4-dinitrophenylosazone of the free acid is a dark yellow substance. It can be kept in the pure state only in complete absence of gaseous ammonia, which is ordinarily present in the laboratory; in the presence of gaseous ammonia the ammonium salt is gradually formed. It was not possible to determine the melting point of the 2,4-dinitrophenylosazone of the free acid accurately because of its rapid conversion to the ammonium salt.

With respect to solubility in water and organic solvents, the dinitrophenylosazone of the free acid is similar to dihydroxytartaric acid p-nitrophenylosazone described above. Its solutions are yellow in color in various shades.

On adding the crystalline osazone to sodium or potassium hydroxide solutions (0.5 N or above) they dissolve readily giving a light violet color. On lowering the hydroxyl ion concentration the color changes to light yellow. Similar results were obtained with aqueous and alcoholic solutions.

The ammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone is rather more soluble in water than the osazone of the free acid; even at room temperature the solutions are colored a fairly bright yellow. Addition of sodium or potassium hydroxide to such solutions causes a color change to light violet. The dry salt

also gives a light violet color to sodium and potassium hydroxide solutions of the above-mentioned concentrations. Aqueous and alcoholic solutions of free dihydroxytartaric acid dinitrophenylosazone and its ammonium salt are considerably more stable than similar solutions of dihydroxytartaric acid p-nitrophenylosazone. They can be kept without loss of indicator properties for several months. The dry ammonium salt is completely stable and does not alter its chemicoanalytical nature on storage.

Dihydroxytartaric acid o-nitrophenylosazone was prepared in a similar manner to that described above for the p-nitro- and 2,4-dinitrophenylosazones.

The pure product was obtained by recrystallizing from boiling ethyl alcohol (96%) with subsequent cooling to 10-15°. On drying in air it is not subject to the action of gaseous ammonia and the ammonium salt can be formed only by treatment with ammonium hydroxide solution as described above for dihydroxytartaric acid p-nitrophenylosazone.

Found %: N 20.30, 20.15. $C_{16}H_{12}O_8N_6$. Calculated %: N 20.18.

Dihydroxytartaric acid o-nitrophenylosazone is an orange colored crystalline substance with a slightly reddish tinge, melting with decomposition at 228°. It is practically insoluble in water. Its solubility in boiling water and organic solvents is of approximately the same order as for the p-nitrophenylosazone. Saturated aqueous solutions have a dull orange-pink color which is unchanged on addition of solutions of alkali hydroxides and carbonates or ammonia. Alcoholic solutions are colored a light orange. On adding them to distilled water or to alkaline solutions they give a dull orange-pink color, on acidification the solutions become pale yellow. The dry product is completely stable; as regards the aqueous and alcoholic solutions, they are more stable than solutions of the p-nitrophenylosazone; their indicator properties do not change for several weeks.

Dihydroxytartaric acid m-nitrophenylosazone was also synthesized in a similar manner to the nitrophenylosazones described above. It was purified by recrystallizing from hot ethyl alcohol (96%).

Found %: N 20.29, 20.22. $C_{16}H_{12}O_8N_6$. Calculated %: N 20.18.

Dihydroxytartaric acid m-nitrophenylosazone is a crystalline substance, bright yellow in color with a slight orange tinge; it melts at 227.5-228°. Its solubility in water and in organic solvents is similar to that of the nitrophenylosazones described above. The solutions are pale yellow in color and do not change under the action of alkalis (of concentrations up to 6 N) or of acids. On keeping the solutions for several months their properties do not change; the dry material is also completely stable.

SUMMARY

The p-nitrophenylosazone, o-nitrophenylosazone, m-nitrophenylosazone and 2,4-dinitrophenylosazone of dihydroxytartaric acid and also the monoammonium salt of dihydroxytartaric acid 2,4-dinitrophenylosazone, not described in the literature, have been synthesized. The compounds obtained were suitably characterized and it was found that all these nitroderivatives, with the exception of dihydroxytartaric acid m-nitrophenylosazone, are capable of undergoing indicator changes.

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INVESTIGATION OF THE RELATIVE REACTIVITY OF THE HYDROXYL GROUPS OF CELLULOSE*

VII. ON THE DISTRIBUTION OF METHOXYL GROUPS IN PARTIALLY METHYLATED CELLULOSE, OBTAINED FROM CELLULOSE TREATED WITH SODIUM ISOAMYLATE

V. Derevitskaia, M. Prokof'eva and Z. Rogovin

From the supposition that there is in the cellulose molecule one hydroxyl group with increased acid properties, the formation of a cellulose alcoholate might be expected not only by the direct action of metallic sodium but also by means of an exchange reaction with an alcoholate of a simple alcohol.

Rassow and Wadewitz [1] were first to attempt to prepare the Na-alcoholate of cellulose in this way. They treated cellulose with solutions of sodium methylate or ethylate in the corresponding alcohols. After the cellulose was treated for 4 hours, the concentrations in the solutions were unchanged. This indicates that under the conditions chosen the Na-alcoholate of cellulose is not formed.

The failure of the above investigators can obviously be explained by the fact that they carried out the reaction in a large excess of the alcohol, which cannot but lead to alcoholysis of the cellulose alcoholate formed. In order to avoid this, one must use Na-alcoholate dissolved in an inert organic solvent. Later [2], by an exchange reaction with thallium alcoholate, cellulose Tl-alcoholate was obtained. This reaction was used for investigation of the structure of cellulose preparations. The cellulose Tl-alcoholate obtained had $\gamma \approx 100$.

In the present work the Na-derivative of cellulose was prepared by the action of sodium isoamylate on cellulose in an inert solvent.

The starting material used for the preparation of the cellulose Na-derivative was cotton cellulose treated with alkali and then by the solvent-displacement method to give an "inclusion" cellulose [3]. The cellulose was treated with a solution of Na-isoamylate [4] in p-xylene, with exclusion of atmospheric moisture and CO_2. The product obtained was washed free from excess Na-isoamylate with xylene, to neutral reaction of the xylene washings. The sodium content of the cellulose Na-derivative was determined by titration [5]. The cellulose Na-derivative obtained had γ 250-260.

It should be noted that the preliminary treatment of the cellulose plays a significant role in the successful conduct of this reaction. Only cellulose regenerated from alkaline cellulose with subsequent inclusion displays sufficient reactivity for this reaction. Preparations of freshly spun viscose rayon and viscose rayon included with benzene without previous swelling in alkali, after treatment with a solution of sodium isoamylate in xylene and subsequent isolation, do not contain sodium.

For the purpose of studying the relative reactivity of the hydroxyl groups of cellulose, samples of the Na-derivative of cellulose of $\gamma \approx 100$-200 were prepared (Table 1).

Two methods were used for preparing the Na-derivative of cellulose of $\gamma \approx 100$.

a) By the action of one mole of sodium isoamylate per mole of cellulose with subsequent removal of

* The 66th communication in the series "Investigation of the structure and properties of cellulose."

TABLE 1

Sample No.	Quantity of Na-isoamylate (in moles per mole of cellulose)	Solvent used for washing the product	γ Na-derivative of cellulose	γ Methyl cellulose
1	7	Benzene	262	–
2	7		257	83.5
3	7		–	130
4	7		–	131
5	7	Isobutyl alcohol	71	72.5
6	7		83.3	81.3
7	7		83.3	77
8	7		72	70.5
9	0.87	Benzene	85	55
10	1		100	89
11	1.23		122	–
12	1.3		130	99.5
13	2		199	106
14	2		199	50.5

TABLE 2

Sample No. (see Table 1)	γ, Methyl cellulose	γ, Trityl ether of methyl cellulose	Number of OCH_3 groups per C_6	Z*
6	81.3	88	12	2.9
7	77	89	11	3
8	70.5	93	7	4.6
9	55	95	5	5
10	89	85	15	2.3
12	99.5	80	20	2
13	106	78	22	1.9

adsorbed isoamylate by washing with xylene. In this case the reaction medium (xylene) and the first portion of xylene used for washing had a neutral reaction, i.e., the sodium was completely combined with the cellulose (Table 1).

b) By washing a cellulose alcoholate of γ 250-260 with dry isobutyl alcohol to neutral reaction of the alcohol washings. Under these conditions an alcoholate with a value of γ near to 100 was always obtained, as in the case of washing the cellulose trialcoholate, prepared from alkaline cellulose in a medium of liquid ammonia, with isobutyl alcohol.

The alcoholate obtained was then methylated with methyl iodide. For determination of the nature of the methoxyl group distribution in the methyl cellulose obtained the number of free, primary hydroxyl groups was determined by tritylation. The results are presented in Table 2.

As is seen from the data in Table 2 the average number of methoxyl groups combined per secondary carbon atom exceeds by 2-5 times the number of methoxyl groups per primary carbon atom. The distribution of methoxyl groups in methyl cellulose is practically independent of the method of preparation of the Na-derivative of cellulose subjected to methylation.

* Z is the ratio of the average number of methoxyl groups combining per secondary carbon atom to the number of methoxyl groups per primary carbon atom.

EXPERIMENTAL

Cotton [6] was used as starting material. Scoured, air-dried cotton was treated [3] with 10% of alkali solution at 5° for 3 hours, the swollen mass was then treated with an equal quantity of 2% alkali solution and after 30 minutes the cotton was filtered off, washed with water, 1% acetic acid and again with water to neutral reaction. Water was displaced from the cotton by methanol, for this purpose the cotton, after water had been squeezed out, was stirred in 1 liter of methanol. After 15 minutes the cotton was squeezed out and steeped in a fresh portion of methanol followed by treatment with a further two fresh portions of dry methanol for 30 minutes each time. Methanol was then rapidly squeezed out from the cotton which was then kept in absolute benzene.

Sodium isoamylate was prepared by the method of Bruhl [4]. A weighed amount of sodium was melted under boiling p-xylene and a fine suspension of sodium in p-xylene was obtained by vigorous shaking. The calculated quantity of isoamyl alcohol was added to the suspension after cooling, the apparatus being protected from moisture and CO_2. By this means Na-isoamylate of high reactivity, free from alcohol of crystallization, was obtained.

A weighed amount of cellulose, previously squeezed out rapidly from benzene, was added to the solution of Na-isoamylate in p-xylene heated to 66-70° (placed in an apparatus fitted with a reflux condenser, stirrer and soda-lime tube). The reaction was carried out for 1 hour at 70° (with continuous stirring) and then for some time at room temperature: for the preparation of the Na-derivative of cellulose of $\gamma \approx 100$ this period was 1 hour, for $\gamma \approx 200 - 3$ hours, and for treatment of cellulose with a large excess of Na-isoamylate – 24 hours. The Na-derivative of cellulose obtained was filtered off rapidly and washed with absolute xylene or isobutyl alcohol, in a flask with a ground-glass stopper, to neutral reaction of the washing liquid. The quantity of combined sodium was determined by titration with 0.01N H_2SO_4 [5].

The Na-derivative of cellulose was methylated with methyl iodide (26 moles per mole of cellulose) in the same apparatus at 42° or in a sealed ampoule at 100° for 3,5 hours. For the determination of methoxyl groups, tritylation of methyl cellulose and analysis of the trityl ether, previously published methods were used [6].

SUMMARY

1. In the reaction between cellulose and Na-isoamylate and subsequent methylation, the secondary hydroxyl groups possess high reactivity.

2. The average number of methoxyl groups combining per secondary carbon atom is approximately 2-5 times greater than the number of methoxyl groups per primary carbon atom.

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THYROID GLAND HORMONES AND THEIR ANALOGS

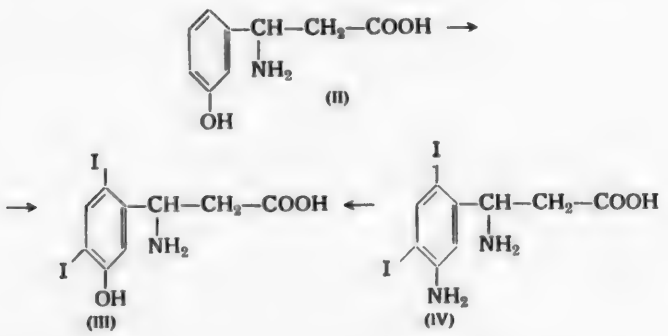
II. SYNTHESIS OF ISOMERS OF BETAZINE

N. N. Suvorov and A. A. Dudinskaia

β-Diiodotyrosine, synthesized by one of us with V. M. Rodionov and V. G. Avramenko [1], which possesses high antithyrotropic (antithyroidal) activity, finds application in medicine for the treatment of thyrotoxicoses, under the name of "Betazine." β-Diiodotyrosine is β-(4-hydroxy-3,5-diiodophenyl)-β-alanine. For the purpose of studying the relationship between antithyroidal activity and chemical structure it was not without interest to synthesize isomers with the phenolic hydroxyl in positions other than that in Betazine.

We have prepared the ortho analog of Betazine, β-(2-hydroxy-3,5-diiodophenyl)-β-alanine, by iodination of β-(2-hydroxyphenyl)-β-alanine which was synthesized by Posner [2] by reacting coumarin with hydroxylamine. It should be noted that demethylation of β-(2-methoxyphenyl)-β-alanine by boiling with hydrobromic acid according to the method developed for β-(4-methoxyphenyl)-β-alanine [1] does not lead to the hydroxyamino acid: on demethylation coumarin is formed with elimination of a molecule of ammonia.

For the synthesis of the meta isomer of Betazine β-(3-hydroxyphenyl)-β-alanine (II), prepared from m-hydroxybenzaldehyde by the V. M. Rodionov reaction, was subjected to iodination with iodine monochloride. It is interesting to note that even in the presence of a large excess of iodinating agent, not the tri- but the diiodo derivative is formed. On the basis of steric considerations the structure β-(3-hydroxy-4,6-diiodophenyl)-β-alanine (III) was ascribed to the latter, this being further confirmed by its preparation through the diazo compound from β-(3-amino-4,6-diiodophenyl)-β-alanine (IV), the structure of which we have proved conclusively [3].



It should be pointed out that the American chemist Jackson [4] recently came to a similar conclusion for a series of amino acids, showing by a rather complicated method, that on iodination of m-tyrosine, β-(3-hydroxy-4,6-diiodophenyl)-alanine is formed.

Information on the physiological activity of the compounds prepared by us will be published elsewhere.

EXPERIMENTAL

β-(2-Hydroxy-3,5-diiodophenyl)-β-alanine (I). β-(2-Hydroxyphenyl)-β-alanine was prepared by the

method of Posner [2]. Yield 60%. M. p. 213.5° (decomp.). To a solution of 3 g of this amino acid in a mixture of 0.6 ml of concentrated hydrochloric acid and 51 ml of water, 5.93 g of iodine monochloride in 12 ml of hydrochloric acid (1:1) was added dropwise at 50°. Heating was continued for a further 2 hours, after which excess iodine was removed with sodium bisulfite. The precipitate that separated (5.6 g) was filtered off and washed with acetone and ether. It consisted of the hydrochloride of of β-(2-hydroxy-3,5-diiodophenyl)-β-alanine.

Found %: Cl (ionic) 7.65, 7.68. $C_9H_9O_3NI_2 \cdot HCl$. Calculated %: Cl (ionic) 7.56.

From a solution of 5.6 g of this hydrochloride in 120 ml of water and 2.1 ml of concentrated hydrochloric acid, free β-(2-hydroxy-3,5-diiodophenyl)-β-alanine (3.6 g) was precipitated (by addition of a saturated solution of sodium acetate at 80°). M. p. 178.5-179° (decomp.).

Found %: I 57.98. $C_9H_9O_3NI_2$. Calculated %: I 58.65.

2-Methoxycinnamic acid. A mixture of 50 g of 2-methoxybenzaldehyde [5], 50 g of malonic acid, 50 ml of dry pyridine and 5 ml of piperidine was refluxed for 4 hours. The reaction mixture was then poured into 500 ml of 12% hydrochloric acid. The precipitate that separated was filtered off, washed with water and crystallized from alcohol. Yield 53 g (81%). M. p. 183-184°. According to the literature [6]; m. p. from 182 to 186°.

β-(2-Methoxyphenyl)-β-alanine was prepared by the following modification of Posner's reaction. A hot solution of 10.5 g of hydroxylamine hydrochloride in 4.2 ml of water was added in one lot to a hot solution of sodium butylate (from 3.48 g of metallic sodium and 70 ml of anhydrous n-butyl alcohol), and the mixture was cooled immediately. The sodium chloride that precipitated was filtered off and to the filtrate was added 5 g of 2-methoxycinnamic acid and the mixture was boiled under reflux for 10 hours. The amino acid was then extracted with water, the water was distilled off in vacuo to dryness and the resinous residue was dissolved in 35 ml of absolute alcohol. The alcoholic solution was treated with activated charcoal, concentrated in vacuo to a small volume and the amino acid was precipitated by the addition of absolute ether. After washing the precipitate with ether 0.65 g of β-(2-methoxyphenyl)-β-alanine was obtained. M. p. 209-210° (decomp.). Posner [7] gives m. p. 209-210°.

Found %: C 61.74, 61.82; H 6.53, 6.69; N 6.76. $C_{10}H_{13}O_3N$. Calculated %: C 61.53; H 6.66; N 7.18.

Demethylation of β-(2-methoxyphenyl)-β-alanine. A solution of 0.37 g of this amino acid in 5 ml of 48% hydrobromic acid was refluxed for 3.5 hours. The hydrobromic acid was distilled off to dryness in vacuo. Addition of 3 ml of water gave a precipitate (0.16 g). After two recrystallizations from water, its melting point was 69-70°; no melting point depression was given on mixing with an authentic sample of coumarin.

β-(3-Hydroxyphenyl)-β-alanine (II). m-Hydroxybenzaldehyde was prepared according to the directions of Woodward [8]. 25 g of this aldehyde, 24 g of malonic acid, 37.5 g of ammonium acetate and 50 ml of n-butyl alcohol were refluxed for 2.5 hours. The precipitate formed was filtered off from the still hot solution and washed with alcohol and ether. Yield 19.5 g (53%). M. p. 222-223° (decomp.). Posner [9] gives m. p. 235-236°.

Found %: N 7.69. $C_9H_{11}O_3N$. Calculated %: N 7.73.

The amino acid obtained was used immediately for iodination.

3.2 g of m-hydroxycinnamic acid of m. p. 190-191° was isolated from the butanol filtrate.

β-(3-Hydroxy-4,6-diiodophenyl)-β-alanine (III). To a solution of 8.8 g of β-(3-hydroxyphenyl)-β-alanine in a mixture of 1.8 ml of conc. HCl and 150 ml of water, a solution of 17.4 g of iodine monochloride in 17 ml of conc. HCl and 17 ml of water was added dropwise at 60° over a period of 30 minutes. Then, after heating the reaction mixture at this temperature for a further 2 hours, 6 ml of a saturated solution of sodium bisulfite was added. The solution was treated with activated charcoal and β-(3-hydroxy-4,6-diiodophenyl)-β-alanine was isolated by adding saturated sodium acetate solution until the mixture was no longer acid to Congo. Yield 16.8 g (80%). After purifying through the difficultly soluble sulfate the melting point was 212-213° (decomp.).

Found %: N 3.13, 3.08; I 58.58, 58.48. $C_9H_9O_3NI_2$. Calculated %: N 3.23; I 58.65.

The O,N-diacetyl derivative was obtained by heating 0.79 g of this amino acid with 7.9 ml of acetic anhydride and 0.2 ml conc. H_2SO_4 for 6 hours at 50-55° with subsequent decomposition of the reaction mixture with 80 ml of ice water. M. p. 235-235.5° (decomp., from a 1:2 mixture of alcohol and water).

Found %: I 49.41. $C_{13}H_{13}O_5NI_2$. Calculated %: I 49.12.

N-Acetyl-β-(3-hydroxy-4,6-diiodophenyl)-β-alanine was prepared by heating a solution of the O,N-diacetyl derivative (0.5 g) in 24 ml of 2N sodium hydroxide for 3.5 hours at 55-60° with subsequent acidification with dilute hydrochloric acid. M. p. 203.5-204.5° (decomp., from a mixture of alcohol and dichloroethane).

Found %: I 53.11. $C_{11}H_{11}O_4NI_2$. Calculated %: I 53.47.

Preparation of β-(3-hydroxy-4,6-diiodophenyl)-β-alanine (III) from β-(3-amino-4,6-diiodophenyl)-β-alanine (IV). To a solution of 4 g of (IV) in a mixture of 35 ml of conc. H_2SO_4 and 40 ml of water, a solution of 0.96 g of sodium nitrite in 7 ml of water was added dropwise at 0-5°. The reaction mixture was maintained at this temperature for 2 hours and was then poured into 40 ml of dilute sulfuric acid (1:1), heated to 135-140°. After heating for 30 minutes at this temperature the solution was cooled, whereby 3.5 g (71%) of the sulfate of β-(3-hydroxy-4,6-diiodophenyl)-β-alanine precipitated. M. p. 228° (decomp., from alcohol).

3.5 g of the sulfate was dissolved in a mixture of 73 ml of water and 27 ml of conc. HCl, the solution was heated to 60° and the free amino acid was precipitated by addition of a saturated solution of sodium acetate. Yield 2.31 g (58%). M. p. 213° (decomp.). No melting point depression was given in admixture with the amino acid prepared by iodination of β-(3-hydroxyphenyl)-β-alanine. The O,N-diacetyl derivatives of these amino acids were also identical.

SUMMARY

1. For the purpose of studying the relationship between antithyrotropic (antithyroidal) activity and chemical structure β-(2-hydroxy-3,5-diiodophenyl)-β-alanine and β-(3-hydroxy-4,6-diiodophenyl)-β-alanine were synthesized, these being the ortho and meta isomers (respectively) of β-diiodotyrosine (Betazine).

2. It was found that on iodination of β-(3-hydroxyphenyl)-β-alanine with iodine monochloride not the triiodo – but the diiodo-substituted derivative – β-(3-hydroxy-4,6-diiodophenyl)-β-alanine is formed.

3. It is shown that boiling β-(2-methoxyphenyl)-β-alanine with hydrobromic acid leads to the formation of coumarin.

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* Original Russian pagination. See C. B. Translation.

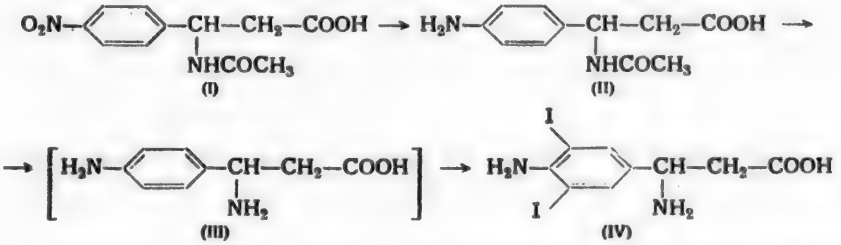
THYROID GLAND HORMONES AND THEIR ANALOGS

III. SYNTHESIS OF AMINO ANALOGS OF BETAZINE

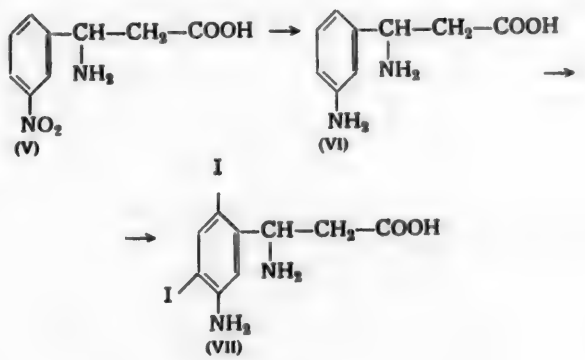
N. N. Suvorov, A. A. Dudinskaia and L. M. Morozovskaia

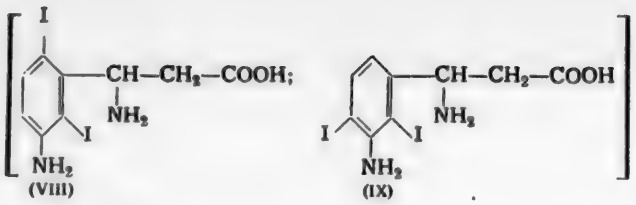
For the purpose of studying the relationship between antithyrotropic (antithyroidal) activity and chemical structure we have synthesized β-(4-amino-3,5-diiodophenyl)- and β-(3-amino-4,6-diiodophenyl)-β-alanine, which are the amino analogs of β-diiodotyrosine (Betazine) [1] and its isomer, β-(3-hydroxy-4,6-diiodophenyl)-β-alanine [2].

We used as starting material for the synthesis of the 4-amino analog of Betazine, N-acetyl-β-4-nitrophenyl-β-alanine (I), previously prepared by one of us [3], which was hydrogenated over Raney nickel to β-4-aminophenyl-β-N-acetylaminopropionic acid (II). The latter was hydrolyzed and the β-4-aminophenyl-β-alanine (III) formed was iodinated with iodine monochloride in dilute hydrochloric acid, without isolation in the pure state, with the formation of the required β-(4-amino-3,5-diiodophenyl)-β-alanine (IV).



For the synthesis of β-(3-amino-4,6-diiodophenyl)-β-alanine (VII) the readily available β-3-nitrophenyl-β-alanine (V) was hydrogenated over Raney nickel and the β-3-aminophenyl-β-alanine (VI) obtained was iodinated with iodine monochloride.

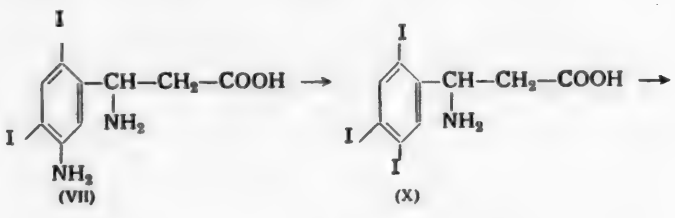




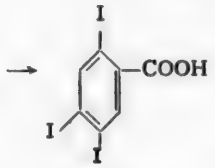
(VIII) (IX)

It is interesting to note that even in the presence of a large excess of iodine chloride it was not possible to prepare the triiodo derivative; evidently this is because an iodine atom cannot take up a position between the aromatic amino group and the β-alanine side chain [2]. Hence, we ascribed structure (VII) to the iodination product, rejecting structures (VIII) and (IX) as improbable.

Conclusive evidence of the structure of the diiodo derivative (VII) was obtained in the following way: the aromatic amino group was substituted by iodine through the diazo compound and the triiodoamino acid (X) obtained was oxidized with potassium permanganate to form a triiodobenzoic acid of m. p. 247-248°. The latter was shown to be identical with 2,4,5-triiodobenzoic acid, described by Wheeler and Johns [4], by direct comparison of the acids themselves and of the ethyl esters which we prepared.



(VII) (X)



(XI)

Information on the physiological activity of the compounds prepared will be published elsewhere.

EXPERIMENTAL

β-4-Aminophenyl-β-N-acetylaminopropionic acid (III). 32.4 g of N-acetyl-β-4-nitrophenyl-β-alanine (I) was hydrogenated in 650 ml of alcohol over Raney nickel at 30 atm and 80° until absorption of hydrogen had ceased completely. The alcohol was distilled off in vacuo and the resinous residue was triturated with ether. The product which crystallized out was washed with the same solvent and recrystallized from absolute alcohol. Yield 18.5 g (64.7%). M. p. 146-147° (decomp.). The product (II) is very soluble in water, moderately soluble in alcohol and has poor solubility in acetone; it is insoluble in ether.

Found %: C 59.42, 59.61; H 6.26, 6.31; N 12.14. $C_{11}H_{14}O_3N_2$. Calculated %: C 59.45; H 6.30; N 12.61.

β-(4-Amino-3,5-diiodophenyl)-β-alanine (IV). 18.5 g of the amino acid (II) was refluxed for 2 hours with 185 ml of dilute (1:1) hydrochloric acid. The reaction mixture was diluted with 278 ml of water and 27.4 g of iodine monochloride in 37 ml of dilute (1:1) hydrochloric acid was added dropwise, with stirring, at 35°. After stirring at this temperature for 3 hours, excess iodine was removed by means of sodium bisulfite. The precipitate that separated on standing was filtered off, dissolved in 250 ml of boiling water, the amino acid precipitated with saturated sodium acetate solution and washed with water, alcohol and ether. Yield 16.4 g (44%). M. p. 222-223° (decomp.). The product is soluble in dilute acids and alkalis. It is insoluble in the usual organic solvents.

Found %: I 57.66, 57.50; H_2O (Fischer) 4.2. $C_9H_{10}O_2N_2I_2 \cdot H_2O$. Calculated %: I 57.44; H_2O 4.0.

0.3 g of the amino acid (IV) was dissolved in a mixture of 0.5 ml of conc. HCl and 5 ml of water. On standing 0.24 g of β-(4-amino-3,5-diiodophenyl)-β-alanine hydrochloride, characterized by a decomposition temperature of about 183° (with evolution of iodine), separated. This compound is moderately soluble in water and dissolves readily in alcohol.

Found %: Cl (ionic) 7.44, 7.50. $C_9H_{10}O_2N_2I_2 \cdot HCl$. Calculated %: Cl (ionic) 7.57.

β-(3-Aminophenyl)-β-alanine (VI). β-3-Nitrophenyl-β-alanine was prepared by Johnson's modification of the V. M. Rodionov reaction in a medium of n-butyl alcohol. Yield 63%. M. p. 236° (decomp.). 10 g of this amino acid was hydrogenated over Raney nickel (2.5 g) in 173 ml of aqueous alcohol (1:1) at 40 atm and 85-90° until absorption of hydrogen had ceased completely. The catalyst was filtered from the hot solution and the filtrate was evaporated in vacuo to small volume. On cooling a precipitate separated which was recrystallized from aqueous alcohol (1:1). Yield 6 g (63%). M. p. 221-222° (decomp.). Posner [5] gives m. p. 228°.

Found %: C 54.43; H 6.91; N 14.05, 13.97; H_2O (Fischer) 9.20. $C_9H_{12}O_2N_2 \cdot H_2O$. Calculated %: C 54.60; H 6.06; N 14.15; H_2O 9.09.

β-(3-Amino-4,6-diiodophenyl)-β-alanine (VII). A solution of 2.57 g of iodine monochloride in a mixture of 2.2 ml of conc. HCl and 2.2 ml of water was added dropwise with stirring over a period of 30 minutes to a solution of 1.3 g of β-(3-aminophenyl)-β-alanine in a mixture of 0.27 ml of conc. HCl and 22 ml of water at 60°. Heating was continued for a further 2 hours, excess iodine was removed with sodium bisulfite, the solution was treated with activated charcoal and the iodinated amino acid was precipitated by means of saturated sodium acetate solution. The precipitate was washed with water, alcohol and ether and purified by reprecipitation from hydrochloric acid as described above. Yield 1.9 g (61%). M. p. 215-216° (decomp.).

Found %: N 6.40, 6.41; I 58.49, 58.05. $C_9H_{10}O_2N_2I_2$. Calculated %: N 6.24; I 58.79.

For the preparation of the dihydrochloride 1.3 g of this amino acid was dissolved in a mixture of 0.5 ml of conc. HCl and 4 ml of water. The solution was treated with activated charcoal and the dihydrochloride was precipitated by addition of 6.5 ml of conc. HCl. Yield 1.1 g (85%). M. p. 183-184° (decomp.).

Found %: Cl (ionic) 13.68, 13.78. $C_9H_{10}O_2N_2I_2 \cdot 2HCl$. Calculated %: Cl (ionic) 14.06.

β-(3,4,6-Triiodophenyl)-β-alanine (X). A solution of 0.64 g of sodium nitrite in 8.3 ml of water was added dropwise to a solution of 2 g of β-(3-amino-4,6-diiodophenyl)-β-alanine in 10.5 ml of water and 4.55 ml of conc. H_2SO_4 at 0-5°. The reaction mixture was stirred at this temperature for 1 hour and then 0.69 g of potassium iodide in 6.3 ml of water was added dropwise to the solution at 0°. After standing at room temperature for 17 hours the mixture obtained was heated to 40° in 5 minutes. Excess iodine was removed with sodium bisulfite and the precipitate was filtered off, washed with water, and dissolved in a mixture of 55 ml of water and 1.5 ml of conc. HCl. The solution was treated with activated charcoal and the amino acid (1.53 g) was precipitated by sodium acetate. After purifying by dissolving in dilute hydrochloric acid, precipitating the hydrochloride with concentrated hydrochloric acid and isolating the free amino acid by means of sodium acetate, β-(3,4,6-triiodophenyl)-β-alanine was obtained with a decomposition temperature of 215° (capillary inserted at 205°, rate of heating 3-4° per minute).

Found %: I 70.21, 70.60. $C_9H_8O_2NI_3$. Calculated %: I 70.11.

Oxidation of β-(3,4,6-triiodophenyl)-β-alanine (X). To a solution of 2 g of (X) in 272 ml of 5% aqueous potassium hydroxide at 40°, 116 ml of a 0.7% solution of potassium permanganate was added dropwise, after which the reaction mixture was heated for a further hour at the same temperature. The temperature was then increased to 75-80° and 230 ml of potassium permanganate solution of the same concentration was added dropwise and heating was continued for 6 hours. Sulfur dioxide was passed through the reaction mixture and the precipitate was filtered off, heated with 25 ml of dilute hydrochloric acid (1:20) and again filtered while still hot. The residue on the filter was stirred and heated with 100 ml of aqueous ammonia (1:2) and filtered, and the filtrate was acidified to Congo with hydrochloric acid. The 2,4,5-triiodobenzoic acid (XI) that precipitated was recrystallized from alcohol. Yield 0.51 g (28%). M. p. 247-248°.

Found %: I 76.61. $C_7H_3O_2I_3$. Calculated %: I 76.20.

No melting point depression was observed on mixing with a sample of 2,4,5-triiodobenzoic acid prepared by the method of Wheeler and Johns [4].

For the preparation of the ethyl ester 1.2 g of our triiodobenzoic acid was dissolved in 62 ml of absolute alcohol containing 0.14 g of potassium hydroxide and the solution was refluxed with 0.2 ml of ethyl iodide for 3.5 hours. M. p. 102-103° (from alcohol).

Found %: I 72.20, 72.68. $C_9H_7O_2I_3$. Calculated %: I 72.15.

A sample of the ethyl ester of the acid synthesized according to Wheeler's method was prepared similarly. The two esters were identical.

SUMMARY

1. The amino analog of Betazine has been synthesized.

2. It has been established that on iodination of β-(3-aminophenyl)-β-alanine, the triiodo derivative is not formed, but β-(3-amino-4,6-diiodophenyl)-β-alanine, the structure of which has been proved conclusively.

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* Original Russian pagination. See C. B. Translation.

N-OXIDES OF THE QUINOXALINE SERIES

II. N-OXIDES OF β-(QUINOXALYL-2)-PROPIONIC AND β-(QUINOXALYL-2)-ACRYLIC ACIDS

A. S. Elina

In a previous communication [1] the properties and method of preparation of mono- and di-N-oxides of quinoxalyl-2-carboxylic acid were described; in that work it was shown that the presence of the electrophilic carboxyl group in the position ortho to the nitrogen of the quinoxaline ring hinders its oxidation.* The resistance to oxidation of the nitrogen (N^1) in quinoxalyl-carboxylic acid is evidently caused by the displacement of its free electron pair in the direction of the carboxyl oxygen.

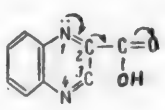
We were interested in the N-oxides of β-(quinoxalyl-2)-propionic acid and its derivatives for the purpose of studying their biological properties.

Since the electrophilic carboxyl group in β-(quinoxalyl-2)-propionic acid is separated from the ring by a two-membered, saturated carbon chain it would be expected that (in contrast to the di-N-oxides of quinoxalyl-2-carboxylic acid) the di-N-oxide of β-(quinoxalyl-2)-propionic acid could be prepared by direct oxidation of the parent acid with hydrogen peroxide.

In fact, β-(quinoxalyl-2)-propionic acid, 1,4-di-N-oxide was obtained in good yield by oxidation of β-(quinoxalyl-2)-propionic acid with 45% H_2O_2 in glacial CH_3COOH. However, it was shown by carrying out the oxidation under milder conditions (5% H_2O_2) that the electrophilic carboxyl group in this case also has some effect on the N^1 of the quinoxaline ring because the mono-N-oxide obtained from this reaction proved to be β-(quinoxalyl-2)-propionic acid 4-N-oxide; this effect is evidently an induction effect.

The position of the N-oxide group was proved by reacting the ethyl ester obtained from the β-(quinoxalyl-2)-propionic mono-N-oxide with $POCl_3$ by analogy with the reaction described previously [1, 2]. Since the compound prepared in this way contained organically-combined chlorine and from analytical data it corresponded to ethyl β-(3-chloroquinoxalyl-2)—propionate, it can be concluded that the parent compound is β-(quinoxalyl-2)-propionic acid 4-N-oxide. It is interesting to note that on hydrogenation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide, the oxygen attached to N^4 is reduced first. The β-(quinoxalyl-2)-propionic acid mono-N-oxide formed on hydrogenation, which by further reduction gives β-(quinoxalyl-2)-propionic acid, is not identical with β-(quinoxalyl-2)-propionic acid 4-N-oxide.

β-(Quinoxalyl-2)-propionic acid was prepared by hydrogenation of the sodium salt of β-(quinoxalyl-2)-acrylic acid [3]. This acid can be prepared by two methods: either by the method, described in the literature, of reacting 2-methyl quinoxaline with chloral with subsequent alkaline hydrolysis of the reaction product [3], or by condensing 2-quinoxalylaldehyde with malonic acid. In the latter case, if the reaction is carried out in glacial acetic acid, quinoxal-2-malonic acid is obtained and is then decarboxylated by heating in quinoline; if, however, the reaction is carried out in pyridine in the presence of piperidine β-(quinoxalyl-2)-acrylic acid can be obtained directly since the quinoxal-2-malonic acid formed as an intermediate product readily decarboxylates under these conditions.



* An error was made in communication [1]: the ethyl ester of quinoxalyl-2-carboxylic acid 4-N-oxide has m. p. 116-117°, and not 156-157° as was stated in communication [1].

β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide was prepared by an analogous reaction from 2-quinoxalylaldehyde 1,4-di-N-oxide, the structure of the former being proved by its oxidation with the calculated quantity of $KMnO_4$ in acetone, to the already known quinoxalyl-2-carboxylic acid 1,4-di-N-oxide [1].

I thank Professor O. Iu. Magidson for the interest that he has taken in this work.

EXPERIMENTAL

β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide. A mixture of 1.9 g of quinoxalyl-2-aldehyde 1,4-di-N-oxide, 1.9 g of malonic acid, 20 ml of dry pyridine and 0.2 ml of piperidine was stirred for 30 minutes at 50° and then at 80° until evolution of CO_2 ceased. The reaction mixture was cooled and β-(quinoxalyl-2)-acrylic acid 1,4-di-N-oxide (1.6 g) was filtered off and then purified either by reprecipitation from an $NaHCO_3$ solution or by crystallization from C_2H_5OH. A bright-yellow crystalline substance of m. p. 219-220° (decomp.), difficultly soluble in organic solvents, liberates iodine from acidic KI solutions (on heating).

Found %: C 56.96, 56.94; H 3.53, 3.67; N 12.16, 12.07. $C_{11}H_8O_4N_2$. Calculated %: C 56.89; H 3.470; N 12.07.

Oxidation of β-(quinoxalyl-2)-acrylic acid di-N-oxide. 0.1 g of the di-N-oxide in 10 ml of acetone was oxidized with an aqueous solution of 0.18 g of $KMnO_4$ at 20-25°. The MnO_2 was filtered off and the filtrate was evaporated down to ¼ volume in vacuo. On acidification a yellow, crystalline material of m. p. 208-209° (from CH_3COOH) separated, that gave a marked melting point depression with the original acid, but gave no depression with quinoxalyl-2-carboxylic acid di-N-oxide [1].

Quinoxalyl-2-malonic acid. A mixture of 5 g of quinoxalyl-2-aldehyde, 5 g of malonic acid and 10 ml of glacial CH_3COOH was stirred for 15 minutes at 63-65°, 0.2 g of activated charcoal was then added and the hot mixture was filtered and allowed to stand for 12 hours at 0°. The quinoxalyl-2-malonic acid that separated, after reprecipitation from $NaHCO_3$ solution was an almost colorless, crystalline material of m. p. 167-168° (decomp.). Yield 3.6 g (46.7%).

Found %: N 11.56, 11.51. $C_{12}H_8O_4N_2$. Calculated %: N 11.47.

β-(Quinoxalyl-2)-acrylic acid. a) Decarboxylation of quinoxalyl-2-malonic acid. A solution of quinoxalyl-2-malonic acid (2 g) in 10 ml of quinoline was heated in a current of CO_2 for 1 hour at 164-166°, then cooled and poured into a solution of $NaHCO_3$. The quinoline layer was separated and washed a few times with $NaHCO_3$ solution. β-(Quinoxalyl-2)-acrylic acid was precipitated from the combined alkaline solutions with hydrochloric acid, after treatment with activated charcoal. Yield of unpurified product 1.38 g. M. p. 205-207°.

b) Condensation of quinoxalyl-2-aldehyde with malonic acid in the presence of piperidine. A mixture of 11 g of quinoxalyl-2-aldehyde, 11 g of malonic acid, 50 ml of pyridine and 1.1 ml of piperidine was heated for 1 hour at 70-75° and 1.5 hours at its boiling point, then cooled and poured, with stirring, into an aqueous $NaHCO_3$ solution and extracted a few times with ether. β-(Quinoxalyl-2)-acrylic acid of m. p. 210-212° was isolated from the alkaline solution (after decolorizing with activated charcoal) by means of hydrochloric acid. Yield 11.6 g (83.4%).

Purification of β-(quinoxalyl-2)-acrylic acid. 11.6 g of the impure acid was added to 25 ml of 15% NaOH solution. 50 ml of absolute C_2H_5OH was added to the reaction mixture which was then allowed to stand for 12 hours at 0°. The sodium β-(quinoxalyl-2)-acrylate was filtered off and dissolved in water. Pure β-(quinoxalyl-2)-acrylic acid was isolated from the solution (after decolorizing with activated charcoal) by means of hydrochloric acid. Yield 11.02 g (95%). M. p. 217-218°.

Found %: C 65.86; H 4.19; N 13.98, 13.92. $C_{11}H_8O_2N_2$. Calculated %: C 65.98; H 4.03; N 13.99.

β-(Quinoxalyl-2)-propionic acid 4-N-oxide. A mixture of 2.5 g of β-(quinoxalyl-2)-propionic acid, 50 ml of CH_3COOH and 12 ml of 5% H_2O_2 was heated for 20 hours at 50°. The reaction mixture was then evaporated to small volume in vacuo at 40° and ether was added until no further turbidity was caused. β-(Quinoxalyl-2)-propionic acid 4-N-oxide, which is a slightly pink, crystalline material, was filtered off. Yield 1.91 g (75%). M. p. 163-164° (from alcohol).

Found %: N 12.89. $C_{11}H_{10}O_3N_2$. Calculated %: N 12.84.

Ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide. 2 ml of H_2SO_4 (d 1.84) was added gradually to 2.4 g of β-(quinoxalyl-2)-propionic acid 4-N-oxide in 46 ml of absolute C_2H_5OH and the mixture was allowed to stand until all the solid material went into solution (2-3 hours). Part of the alcohol was then distilled off in vacuo and the residue was poured into an $NaHCO_3$ solution containing pieces of ice. The ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide was extracted with ether. The ethereal solution was dried and the ether distilled off. The residue was crystallized from aqueous C_2H_5OH. Pale-yellow needles of m. p. 73-74°. Yield 2.0 g (68.5%).

Found %: C 63.67; H 5.73; N 11.51. $C_{13}H_{14}O_3N_2$. Calculated %: C 63.4; H 5.73; N 11.37.

Ethyl β-(3-chloroquinoxalyl-2)-propionate. 0.50 g of the ethyl ester of β-(quinoxalyl-2)-propionic acid 4-N-oxide was added gradually with cooling to 2.5 ml of $POCl_3$. The solution was then heated at 80-85° for 40 minutes, cooled and poured onto ice, and after standing for an hour it was extracted with ether. After removing the ether 0.42 g of ethyl β-(3-chloroquinoxalyl-2)-propionate remained. A slightly pink, crystalline material of m. p. 78-79° (from aqueous ethanol); insoluble in water, dilute acids and alkalis, soluble in concentrated acid solutions.

Found %: N 10.4; Cl 13.5. $C_{13}H_{13}O_2N_2Cl$. Calculated %: N 10.58; Cl 13.39.

β-(Quinoxalyl-2)-propionic acid 1,4-di-N-oxide. a) A mixture of 83 ml of CH_3COOH, 24 ml of 30% perhydrol and 20 ml of acetic anhydride was heated for 3 hours at 50°; 5 g of β-(quinoxalyl-2)-propionic acid was then added and the mixture was kept at 50° for 20 hours. The reaction mixture was evaporated to a small volume in vacuo and 4.15 g (71.5%) of β-(quinoxalyl-2)-propionic acid 1,4 di-N-oxide was isolated by adding ether to the residue. A yellow, crystalline substance of m. p. 184-185° (decomp., from alcohol). Liberates iodine from acidified KI solutions on heating.

Found %: C 56.23; H 4.55; N 12.16, 12.07. $C_{11}H_{10}O_4N_2$. Calculated %: C 56.4; H 4.3; N 11.96.

b) A mixture of 5 ml of CH_3COOH, 3 ml of 30% perhydrol and 1.5 ml of acetic anhydride was heated for 3 hours at 40-50°, then 0.3 g of β-(quinoxalyl-2)-propionic acid 4-N-oxide was added and the mixture was maintained at 50° for 20 hours. The reaction mixture was evaporated to a small volume in vacuo, after which ether was added until no more turbidity appeared and 0.2 g of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide precipitated, which melted at 184-185° (decomp.) after reprecipitation from $NaHCO_3$ solution, and gave no melting point depression with β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide prepared by direct oxidation of β-(quinoxalyl-2)-propionic acid.

Reduction of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide. 0.5 g of the 1,4-di-N-oxide was dissolved in 12 ml of 8% aqueous NaOH, 0.5 g of moist nickel catalyst was added and the reaction mixture was shaken in a current of hydrogen. Hydrogenation was discontinued when 50 ml of hydrogen had been absorbed. The catalyst was filtered off and β-(quinoxalyl-2)-propionic acid 1-N-oxide (0.30 g) was isolated from the filtrate by addition of hydrochloric acid. A pale-yellow, crystalline material of m. p. 203-204° (decomp., from alcohol).

Found %: C 60.62, 60.79; H 4.65, 4.74; N 12.77. $C_{11}H_{10}O_3N_2$. Calculated %: C 60.54; H 4.62; N 12.84.

0.05 g of β-(quinoxalyl-2)-propionic acid was salted out from the acidified solution by addition of NaCl.

Reduction of β-(quinoxalyl-2)-propionic acid 1-N-oxide. To a solution of 0.15 g of the N-oxide in 4 ml of 2% NaOH solution, 0.1 g of moist nickel catalyst was added and the mixture was shaken in a stream of hydrogen. 15 ml of hydrogen was absorbed. The catalyst was filtered off and β-(quinoxalyl-2)-propionic acid (0.08 g) was precipitated by addition of hydrochloric acid. M. p. 118-119°; a mixed melting point with β-(quinoxalyl-2)-propionic acid prepared in the usual way showed no depression.

SUMMARY

1. It has been established that on oxidation of β-(quinoxalyl-2)-propionic acid with dilute hydrogen peroxide in acetic acid, a mono-N-oxide is formed, oxidation occurring at the nitrogen in position 4, and when more concentrated hydrogen peroxide solutions are used, oxidation of the second nitrogen also takes place with the formation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide.

2. It has been shown that on hydrogenation of β-(quinoxalyl-2)-propionic acid 1,4-di-N-oxide the N^4 oxygen is reduced first, followed by the N^1 oxygen.

3. A method of preparation of β-(quinoxalyl-2)-acrylic acid from quinoxalyl-2-aldehyde and malonic acid is proposed.

4. β-(Quinoxalyl-2)-acrylic acid 1,4-di-N-oxide has been prepared by this method from quinoxalyl-2-aldehyde 1,4-N-oxide and malonic acid.

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CARDIAC GLYCOSIDES OF THE SEEDS OF WORM-SEED MUSTARD

(Erysimum cheiranthoides L.)

N. P. Maksiutina

Worm-seed mustard (Erysimum cheiranthoides L.), is an annual herbaceous plant that grows in all parts of of the European territory of the Soviet Union, in Siberia and in the Far East. The leaves of worm-seed mustard have long been used in popular medicine as a powerful diuretic. A number of authors [1-4] who have studied the infusion and extraction of worm-seed mustard classify it as a plant possessing considerable cardiac activity. Investigators [1-9] studying ultimate preparations of worm-seed mustard observe that these preparations are similar to strophanthin in pharmacological and chemical activity. P. M. Loshkarev [9] in describing the cardiotonically active species of erysimum, regards worm-seed mustard as a valuable medical plant that can serve as an indigenous source for the production of a cardiac preparation very close in properties to strophanthin.

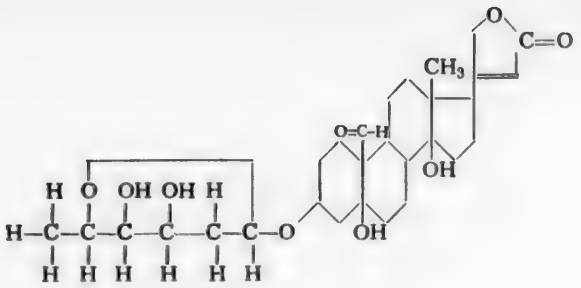
In spite of the considerable interest in this plant, no individual active substance has been isolated up to the present time. The first, preliminary communication of Mushinskii and co-workers [10] on the isolation of three glycosides from the seeds of worm-seed mustard did not appear until 1956. The glycosides were isolated by the method of Reichstein through the products of acetylation and had: first – m. p. 148-150°, second – m. p. 190-195° and third – m. p. 218-221°. All three glycosides did not belong to the main class of physiologically active components since they showed very low biological activity; the activity of the initial chloroform-alcohol extract from which they were prepared was 2-8 times greater.

The object of the present work was to investigate the glycoside composition of the seeds of worm-seed mustard and to isolate the more active glycosides in the crystalline form.

In an investigation of the glycoside composition of the seeds by the method of paper-chromatography, we discovered seven glycosides in more or less significant quantity and three as small traces. We succeeded in isolating two crystalline glycosides of m. p. 196-197° and 224-226° by the method of mild fermentational degradation. The first glycoside named "erysimotoxin" was obtained in a yield of 0.1%; its biological activity in the cat was 0.095 mg/kg body weight*. The second glycoside named "erysin" was obtained in a yield of 0.012%; its biological activity in the cat was 0.11 mg/kg body weight. Both glycosides have high biological activity exceeding in strength the activity of strophanthin, cymarin, digitoxin, convalloside (convallotoxin) and other known cardiac glycosides. The high biological activity and comparatively large yield of erysimotoxin suggest that it is the main active substance of the seeds of worm-seed mustard. According to the physicochemical data obtained, erysimotoxin has one aldehyde group, two secondary and two tertiary hydroxyl groups and an unsaturated, five-membered lactone ring. The aglycon, according to its properties and R_f value, is similar to strophanthidin. The sugar component of erysimotoxin is represented by one molecule of a 2-desoxy sugar. Comparison of the sugar obtained with the known 2-desoxy sugars on paper chromatograms established that it is identical with digitoxose.

On the basis of investigations carried out on the glycoside, its acetyl derivative, the aglycon and the sugar component, the structure given on the next page can be put forward for erysimotoxin.

* The biological activity was measured in the pharmacological laboratory of our Institute.



Erysin in chemical respects is also a steroid glycoside with a five-membered lactone ring without a 2-desoxy sugar.

EXPERIMENTAL

Preparation of erysimotoxin and erysin. 2 kg of seeds was steeped in 2 liters of water and left to stand for two days at room temperature for autolysis. The swollen seeds were ground and the glycosides were extracted from them with a five-fold quantity of water. The seeds were separated in a centrifuge and the aqueous extract was diluted with an equal volume of ethyl alcohol for the precipitation of impurities. The sediment was separated and the filtrate was purified with lead hydroxide [from 1 kg of Pb $(CH_3COO)_2 \cdot 5H_2O$]. The glycosides from the purified filtrate were extracted a few times with chloroform, the extracts evaporated down in vacuo, the residue dissolved in 200 ml of a mixture of chloroform and alcohol (98:2) and the solution chromatographed on aluminum oxide. On elution of the column with a mixture of chloroform and alcohol (98:2) five zones were found, easily visible in UV light. The zones were separated and the glycosides from each zone desorbed separately with ethyl alcohol, the alcohol distilled off and the residues dissolved in alcohol or hot water and left to crystallize. The glycoside erysimotoxin was obtained from the two lower zones in a yield of 0.1%. From the upper zone the other glycoside called erysin was obtained; its yield was 0.012%.

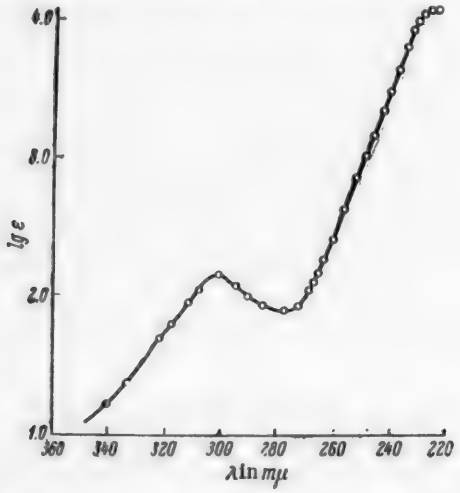


Fig. 1. UV absorption spectrum of erysimotoxin.

Erysimotoxin crystallizes from dilute alcohol in the form of colorless, long plates of m. p. 196-197°. It is readily soluble in dilute alcohol, chloroform, hot water and pyridine, difficultly soluble in cold water and insoluble in ether and petroleum ether. Erysimotoxin gives positive Legal, Liebermann and Keller-Kiliani reactions; in concentrated sulfuric acid it dissolves with a brown coloration, turning to green then to blue.

$[\alpha]^{20}D$ + 26.77 ± 2° (in alcohol).

For analysis the erysimotoxin was dried in high vacuum for 2 hours at 80°.

Found %: C 63.02; H 8.08. M 551.0. $C_{29}H_{42}O_9 \cdot H_2O$. Calculated %: C 62.97; H 7.96. M 552.63.

The absorption spectrum of erysimotoxin (Fig. 1) has two maxima: λ_{max} 302 mμ (log ε 2.17), λ_{max} ~ 220 mμ (log ε 4.08).

Erysimotoxin acetate. 0.2 g of erysimotoxin was acetylated with acetic anhydride in pyridine for 48 hours at 30°. After removal of the solvent the acetate crystallized from a mixture of pyridine and water in the form of thick plates of m. p. 232-235°. It is readily soluble in chloroform and alcohol and very difficultly soluble in

water. In concentrated sulfuric acid the acetate dissolves with a blue-green coloration, changing to emerald-green then to yellow and blue.

$[\alpha]^{22}D$ + 40.6 ± 2° (in chloroform).

The sample was analyzed after drying in high vacuum at 100° for 3 hours.

Found %: C 64.11; H 7.56. M 619.3. $C_{33}H_{46}O_{11}$. Calculated %: C 64.03; H 7.53. M 618.70.

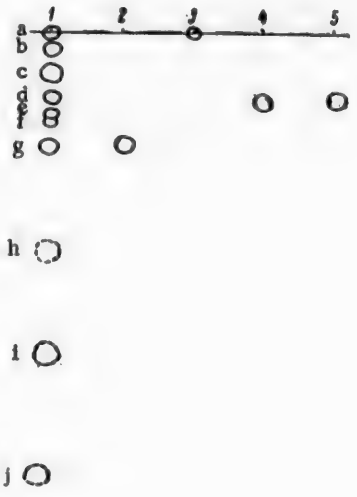


Fig. 2. Positions of the glycoside and aglycon spots on a paper chromatogram: 1) purified extract of worm-seed mustard seeds; 2) erysimotoxin; 3) erysin; 4) erysimotoxigenin; 5) strophanthidin R_f values: a – 0.00, b – 0.03, c – 0.076, d – 0.12, e – 0.15, f – 0.166, g – 0.21, h – 0.40, i – 0.58, j – 0.85.

Fig. 3. Position of sugar spots on a paper chromatogram: 1) sugar of m. p. 97-99°; 2) digitoxose (R_f 0.79).

Acid hydrolysis of erysimotoxin. 0.2 g of erysimotoxin was hydrolyzed with 0.3N H_2SO_4 solution at room temperature. Hydrolysis took place very rapidly: after only an hour in the acid solution the aglycon began to crystallize in the form of thick plates and nodules. On diluting the acid hydrolyzate with an equal volume of water, the aglycon precipitated out completely. After recrystallizing the aglycon from alcohol, it had m. p. 174-175°, but from a mixture of chloroform and benzene – 232-233°. The aglycon dissolves readily in chloroform and alcohol, with difficulty in benzene and is practically insoluble in water. The aglycon gives positive Legal and Liebermann reactions and a negative Keller-Kiliani reaction. In concentrated sulfuric acid it dissolves with a yellow coloration. It isomerizes in an alkaline medium.

$[\alpha]^{21}D$ + 46.3 ± 2° (in alcohol).

Found %: C 68.32; H 7.96. M 404.5. $C_{23}H_{32}O_6$. Calculated %: C 68.29; H 7.97. M 404.

The acidic, aqueous liquor, after separation of the aglycon, was treated twice with 40 ml of a mixture of alcohol and chloroform (1:2), evaporated down a little in vacuo and neutralized with $BaCO_3$. The precipitate was filtered off after thickening with a little kieselguhr and the filtrate was evaporated in vacuo. The residue was dissolved in 5 ml of absolute alcohol, the solution filtered and the alcohol distilled off. The purified syrup was dissolved in a small quantity of dry acetone, diluted with ether and crystallized at 0°. On standing for 46 hours crystals of a sugar of m. p. 97-99° appeared. The crystals gave a positive Keller-Kiliani reaction indicating the presence of a 2-desoxy sugar.

Erysin crystallizes from water in the form of short plates, collected together in clusters, of m. p. 224-226°. It dissolves readily in alcohol and hot water, with difficulty in chloroform and is insoluble in ether. In concentrated sulfuric acid it dissolves with an orange coloration changing to brown and yellow. Erysin gives positive Legal and Liebermann reactions and reduces Fehling's reagent only after acid hydrolysis. The Keller-Kiliani reaction is negative.

Investigation of the glycoside composition of the seeds by the method of paper chromatography. For this investigation an extract from the seeds containing all the glycosides, the glycosides erysimotoxin and erysin,

and the aglycons strophanthidin and erysimotoxigenin were taken. Separation was carried out on chromatographic paper (Leningrad factory) in the system formamide-chloroform. The results are shown in Fig. 2, from which it is seen that the purified extract of worm-seed mustard seeds gives ten glycoside spots. Three of these glycosides are present in insignificant quantity (R_f 0.4, 0.58 and 0.85), two have been isolated in crystalline form (R_f 0.00 and 0.21) and the remaining five glycosides (R_f 0.03, 0.076, 0.12, 0.15 and 0.166) have not yet been isolated.

On comparing the aglycon of erysimotoxin (erysimotoxigenin) with strophanthidin, we obtained spots on the chromatogram of almost identical R_f values (0.125 and 0.12). The paper-chromatographic data and other physicochemical properties of the aglycon of erysimotoxin enable the assumption to be made that it is very close to strophanthidin and is possibly identical with it.

For identification of the sugar of m. p. 97-99° obtained from the acid hydrolysis of erysimotoxin, it was chromatographed on paper in the system n-butanol-pyridine-water (3:2:1.5). Aniline phthalate in n-butanol was used to develop the spots. A solution of digitoxose was used as a "control." The results shown in Fig. 3 provide a basis for the conclusion that the sugar obtained by us is identical with digitoxose.

SUMMARY

1. From the seeds of worm-seed mustard two new glycosides with cardiac activity – erysimotoxin and erysin – have been isolated.

2. The main physicochemical properties of the glycosides have been determined. The acetate of erysimotoxin and the products of acid hydrolysis have been obtained.

3. The glycoside composition of worm-seed mustard seeds has been investigated by the method of paper chromatography. Ten glycosides were discovered in the seeds.

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INVESTIGATION OF COMPLEX-FORMATION IN SOLUTIONS OF TERNARY SYSTEMS BY PHYSICOCHEMICAL ANALYSIS METHODS

IX. THE SYSTEMS $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Br and $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Cl

E. Ia. Gorenbein and V. N. Danilova

In our previous investigations it was shown that aluminum bromide with ethyl ether in ethylene bromide, benzene, bromobenzene and chlorobenzene forms two compounds – $AlBr_3 \cdot (C_2H_5)_2O$ and $Al_2Br_6 \cdot (C_2H_5)_2O$ [1-3]. These compounds are good electrolytes even for solvents with a low dielectric constant. It seemed of interest to discover whether aluminum bromide forms molecular compounds of a similar composition with other ethers and to what extent the nature of the solvent affects the complex formation process. In addition to this there was the problem of verifying the rule [4] that if two nonelectrolytes form two or more electrolytes, then examination of the viscosity characteristics as a method of physicochemical analysis will indicate the compound that has the highest conductivity in the given medium.

In the present communication we present the results of investigation of the reaction of isoamyl ether with aluminum bromide in chlorobenzene and bromobenzene as solvents.

EXPERIMENTAL

Starting materials and method of investigation. Chlorobenzene and bromobenzene were purified as described previously [3]. Aluminum bromide was synthesized from bromine and metallic aluminum [5]; isoamyl ether was prepared according to Gatterman [6]; the carefully purified product was dried initially over fused calcium chloride, then dried and distilled over metallic sodium. The materials obtained were stored in sealed ampoules.

TABLE 1

Viscosity, Density and Electrical Conductivity of the System $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Br, at 15°.

Molar ratio $\frac{AlBr_3 + (C_5H_{11})_2O}{C_6H_5Br}$	$AlBr_3$ in the mixture $AlBr_3 + (C_5H_{11})_2O$ (mole %)	d_4^{15}	$\eta \cdot 10^2$	$\varkappa \cdot 10^4$
0.1504	0	1.3432	1.193	—
0.1495	18.92	1.4070	1.375	—
0.1495	29.38	1.4459	—	0.36
0.1498	40.44	1.4750	1.535	0.69
0.1502	43.99	1.4903	—	1.07
0.1509	44.51	—	—	1.05
0.1503	48.77	—	—	0.78
0.1496	50.11	1.5094	1.613	0.23
0.1599	50.18	—	—	0.24
0.1480	54.49	1.5260	1.647	1.39
0.1483	60.20	1.5484	1.672	1.78
0.1499	64.96	1.5660	1.652	1.45
0.1475	72.51	1.5819	1.642	—
0.1499	75.41	1.5894	—	0.84
0.1481	78.04	1.5982	1.638	0.77
0.1510	98.55	1.6753	1.542	0.05
0.1510	100	1.6623	1.520	—

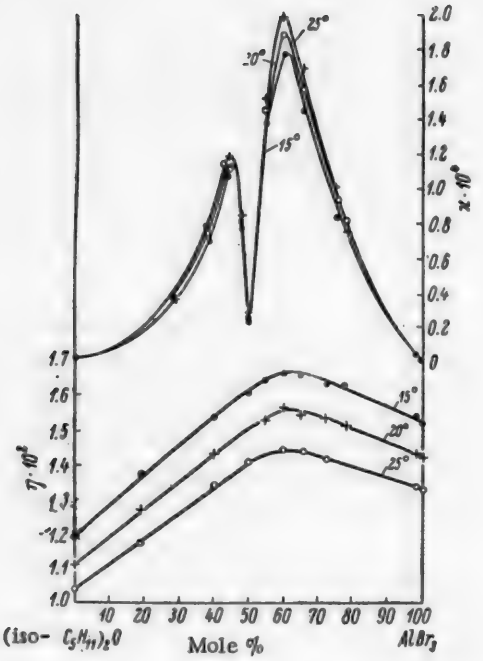


Fig. 1. Variation of viscosity and specific electrical conductivity of the system $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$ with ratio of $AlBr_3$ and $(C_5H_{11})_2O$.

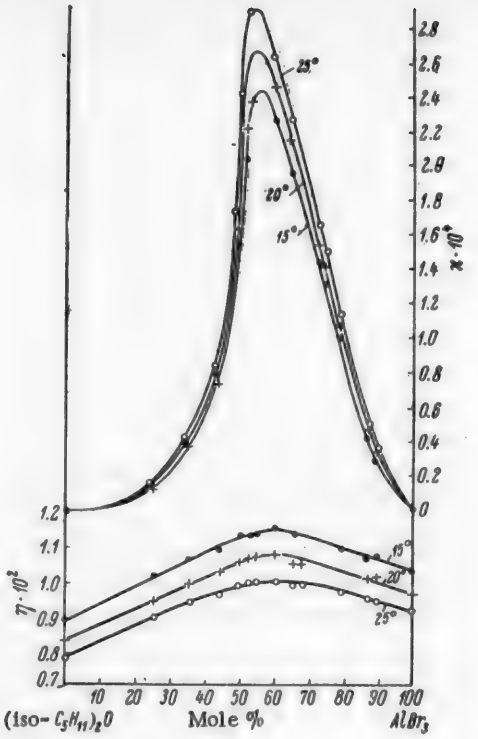


Fig. 2. Variation of viscosity and specific electrical conductivity of the system $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Cl$ with ratio of $AlBr_3$ and $(C_5H_{11})_2O$.

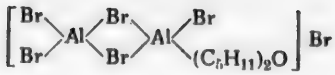
Solutions of isomolar concentration were prepared as described in a previous communication [3].

The viscosity of the solutions was measured with a viscometer [7], and the electrical conductivity and density as described earlier [8, 9]. Investigations were carried out at 15, 20 and 25°.

System $AlBr_3$–$(iso\text{-}C_5H_{11})_2O$–$C_6H_5Br$. Solutions of $AlBr_3$ in bromobenzene are practically nonconducting and according to the results of thermal analysis these components, do not form a compound [10]. On dissolving $AlBr_3$ in C_6H_5Br, a slight evolution of heat is observed and the solution becomes red. Addition of isoamyl ether to this solution is accompanied by a marked heat effect. The color of the solution changes from cherry red to light brown. We studied the viscosity, electrical conductivity and density of this system at isomolar concentrations of $AlBr_3$ + $(iso\text{-}C_5H_{11})_2O$ equal to 0.15 mole per mole of bromobenzene. The results of measurements at 15° are given in Table 1 and the other results are presented graphically.

Figure 1 shows the variation of viscosity and specific electrical conductivity with concentration of the components $AlBr_3$ + $(iso\text{-}C_5H_{11})_2O$, the mole sum of which is taken as 100%. The viscosity maximum corresponds approximately to the compositions of the compound $Al_2Br_6 \cdot (C_5H_{11})_2O$. The specific electrical conductivity curve has two maxima and a minimum. The first specific electrical conductivity maximum and the minimum correspond to $AlBr_3 \cdot (iso\text{-}C_5H_{11})_2O$. Here, evidently, as in previous cases [2, 3], the formation of a minimum is connected with the conversion of the electrolyte $[AlBr_2 2(C_5H_{11})_2O]\,[AlBr_4]$ to the nonelectrolyte $[AlBr_3(C_5H_{11})_2O]$ according to the scheme $[AlBr_2 2(C_5H_{11})_2O]\,[AlBr_4] \rightleftharpoons 2[AlBr_3(C_5H_{11})_2O]$.

On further increase in concentration of aluminum bromide interaction between $[AlBr_3(C_5H_{11})_2O]$ and $AlBr_3$ takes place with the formation of the compound $Al_2Br_6 \cdot (C_5H_{11})_2O$, which is an electrolyte; its composition can be represented by the formula



This compound corresponds to the second conductivity maximum. It is characteristic that the effect of temperature on electrical conductivity shows up in the region of the electrolyte formed in highest concentration in the solution.

The coincidence of the second conductivity maximum with the viscosity maximum is in full agreement with the above mentioned rule: if two substances form two or more electrolytes, then examination of viscosity characteristics as a method of physicochemical analysis will indicate the compound that has the highest conductivity [4].

TABLE 2

Viscosity, Density and Electrical Conductivity of the System $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Cl at 15°.

Molar ratio $\frac{AlBr_3+(C_5H_{11})_2O}{C_6H_5Cl}$	$AlBr_3$ in the mixture $AlBr_3+(C_5H_{11})_2O$ (mole %)	d_4^{15}	$\eta \cdot 10^3$	$\varkappa \cdot 10^4$
0.1500	0	1.0385	0.892	—
0.1498	25.11	1.1072	1.022	0.14
0.1501	35.54	1.1388	1.059	0.39
0.1493	43.92	1.1520	1.096	0.75
0.1518	49.70	1.1780	1.131	1.56
0.1498	52.59	1.1883	1.133	2.06
0.1467	54.18	1.1920	1.157	2.39
0.1498	60.14	1.2090	1.154	—
0.1358	61.42	—	—	2.28
0.1460	65.41	1.2230	1.142	1.96
0.1496	67.70	1.2304	—	—
0.1480	73.96	—	—	1.45
0.1491	75.73	—	—	1.33
0.1485	79.42	1.2630	1.096	1.01
0.1501	87.02	1.2855	1.072	0.44
0.1499	89.32	1.2920	1.076	0.31
0.1496	100	1.3234	1.028	—

$AlBr_3$-(iso-$C_5H_{11})_2O$-C_6H_5Cl. No molecular compounds of $AlBr_3$ and chlorobenzene are known. On adding isoamyl ether to a chlorobenzene solution of aluminum bromide, considerable evolution of heat is observed. The color of the solution changes from faint yellow to brown and at ether concentrations greater than 50%, the solution becomes cherry red. Chlorobenzene solutions of $AlBr_3$ and isoamyl ether are more stable than the corresponding bromobenzene solutions

In Table 2 and in Figure 2 results of the investigation of viscosity, electrical conductivity and density of the system $AlBr_3$-(iso-$C_5H_{11})_2O$-C_6H_5Cl at the same isomolar concentrations and temperatures as for the system with C_6H_5Br are given.

The viscosity and specific electrical conductivity curves have a single maximum which evidently indicates the formation of the compound Al_2Br_6–$(C_5H_{11})_2O$. Although the left branch of the specific electrical conductivity curve can be regarded as S-shaped, the inflection in which might correspond to the compound $AlBr_3 \cdot (C_5H_{11})_2O$, this inflection is too weakly expressed to enable any conclusion to be drawn. Obviously the difference in the nature of the specific electrical conductivity curves characteristic of the interaction of the same two compounds in the two solvents (C_6H_5Br and C_6H_5Cl) must be connected with the nature of the solvents themselves.

It can therefore be considered that $AlBr_3$ and isoamyl ether in bromobenzene as solvent form two complex compounds, and in chlorobenzene only one.

SUMMARY

1. The viscosity and electrical conductivity of the system $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Br and $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Cl at 15, 20 and 25° has been studied.

2. It has been found that under the experimental conditions aluminum bromide and isoamyl ether in bromobenzene forms two compounds $AlBr_3 \cdot (C_5H_{11})_2O$ and $Al_2Br_6 \cdot (C_5H_{11})_2O$, and in chlorobenzene one compound $Al_2Br_6 \cdot (C_5H_{11})_2O$.

3. It is shown that for the section of the system $AlBr_3$–(iso-$C_5H_{11})_2O$–C_6H_5Br studied the rule holds that if two nonelectrolytes interact to form two or more electrolytes, then examination of the viscosity characteristics as a method of physicochemical analysis will indicate which compound in the solution has the highest conductivity.

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THE IRREVERSIBLE-RECIPROCAL SYSTEM FROM SODIUM AND POTASSIUM FORMATES AND THIOCYANATES

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A study of reciprocal systems from salts of aliphatic acids and sodium and potassium thiocyanates is undertaken for the purpose of determining the effect of the structure of the aliphatic acid salt radical on the processes in melts of the salts. The binary system NaCNS–KCNS serves as one of the sides of the composition diagram of the systems being studied; the sodium and potassium salts of the homologous series of aliphatic acids, both with straight and branched carbon chains in the radical, are taken as the other salts. In the present work the reciprocal system Na, K || HCOO, CNS is studied.

Sodium thiocyanate does not undergo polymorphic transformations; it is thermally stable up to 500° [1, 2]. Potassium thiocyanate is thermally stable up to 400° [2]; at 142.5° a polymorphic transformation occurs [3]. Sodium formate is stable up to 310° [4]; a polymorphic transformation, as was shown by one of us [5], takes place at 242°. At 370° potassium formate begins to decompose and at 470° decomposition proceeds very rapidly [6]. While investigating the heating of potassium formate with the aid of a differential thermocouple, one of us found that it undergoes polymorphic transformations at 60, 135 and 157° [5].

The heats of formation are known for all the components of the present system: (in kcal/equiv.): NaCNS – 40.36, KCNS – 47.40, HCOONa – 157.7, HCOOK – 160.7 [7]. From these figures it would be expected that the equilibrium in this system would be displaced toward the side of the pair HCOONa and KCNS: HCOOK + + NaCNS ⟶ HCOONa + KCNS + 4.00 kcal.

EXPERIMENTAL

The work was carried out by the visual-polythermic method according to the usual method, a detailed description of which we have given previously [8]. Commercial C.P. or "Pure for Analysis" preparations of the salts were taken for this work and recrystallized – the thiocyanates from alcohol, sodium formate from water and potassium formate from formic acid. The excess acid was removed according to Schlesinger and Martin [9]. The melting points of the components of the system were: sodium thiocyanate 311°, potassium thiocyanate 177°, sodium formate 258° and potassium formate 167°.

Binary Systems

The system NaCNS-KCNS has a simple eutectic [1]. The branches of the melting-point curve intersect, according to our results, at 126° and 74% KCNS (Fig. 1).

The system HCOONa-HCOOK. Three branches of the melting-point curve intersect in two eutectic points – at 168° and 49.5% HCOOK and at 167° and 96% HCOOK. The composition of the compound formed is 3HCOOK·HCOONa (Fig. 1).

The system KCNS-HCOOK has been investigated by us for the first time. Two branches of the melting point curve intersect in a eutectic point at 83° and 52.5% HCOOK (Fig. 1).

The system NaCNS-HCOONa was first investigated by one of us [8]. Two branches of the melting-point curve intersect in a eutectic point at 189° and 62% HCOONa (Fig. 1).

Numerical data are given in Table 1.

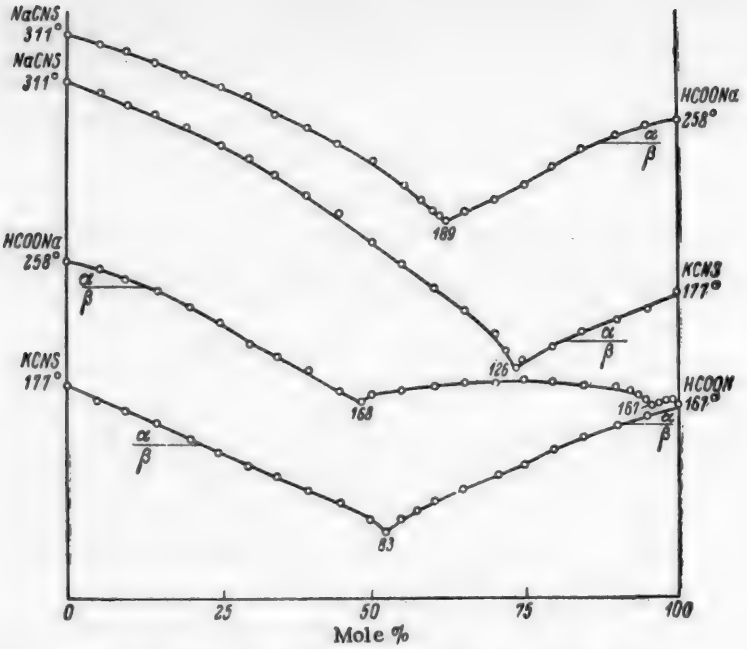

Fig. 1. Melting point diagram of the binary systems.

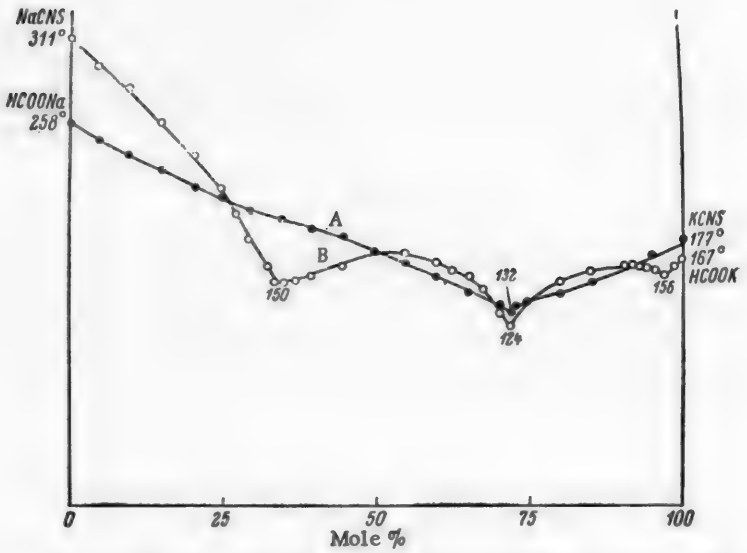

Fig. 2. Diagonal sections of the system: A) stable diagonal section; B) metastable diagonal section.

TABLE 1

Binary Systems

$NaCNS$–KCNS		HCOONa–HCOOK		KCNS–HCOOK		$NaCNS$–HCOONa	
KCNS (moles %)	temp.	HCOOK (moles %)	temp.	HCOOK (moles %)	temp.	HCOONa (moles %)	temp.
0	311°	0	258°	0	177°	0	311°
5	304	5	252	5	168	5	306
10	298	15	240	10	162	10	298
15	292	20	232	15	156	15	290
20	282	35	198	20	145	20	283
25	272	40	186	25	135	25	278
30	262	45	176	30	128	30	269
35	251	47.5	170	35	119	35	259
40	238	49.5	168	40	111	40	251
45	224	52.5	173	45	102	45	237
50	211	55	175	50	91	50	228
55	195	60	176	52.5	83	55	210
60	178	65	179	55	89	60	195
65	162	70	180	57.5	96	62	189
70	142	75	182	60	104	65	195
72.5	131	80	181	65	112	70	202
74	126	85	180	70	119	75	216
75	127	90	179	75	129	80	225
80	139	93	177	80	137	85	239
85	150	94	173	85	147	90	246
90	158	95	171	90	155	95	256
95	168	96	167	95	162	100	258
100	177	97	168	100	167		
		99	169				
		100	167				

TABLE 2

Diagonal sections

Stable diagonal section HCOONa–KCNS		Metastable diagonal section $NaCNS$–HCOOK			
KCNS (moles %)	temp.	HCOOK (moles %)	temp.	HCOOK (moles %)	temp.
0	258°	0	311°	72.5	126°
5	247	5	297	75	139
10	236	10	281	80	152
15	227	15	259	85	159
20	218	20	241	90	165
25	212	25	215	92.5	164
30	203	27.5	201	95	162
35	194	30	183	96	158
40	189	32.5	163	96.4	156
45	183	34	150	97	158
50	174	35	151	98	160
55	166	37.5	153	100	167
60	161	40	156		
65	147	45	165		
70	135	50	174		
71.5	132	55	172		
75	139	60	165		
80	145	62.5	159		
85	153	65	154		
90	161	67.5	146		
95	170	70	131		
100	177	72	124		

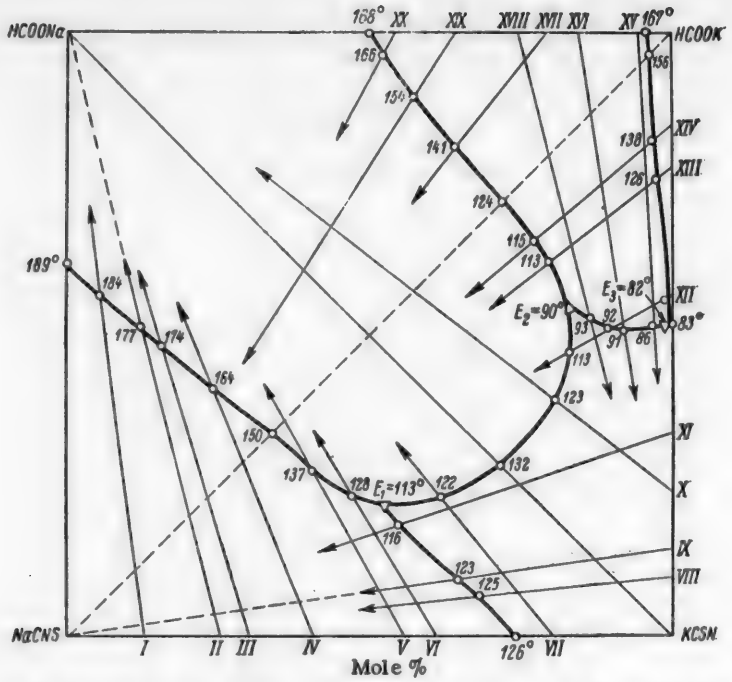

Fig. 3. Positions of the internal sections in the system Na, K ‖ HCOO, CNS.

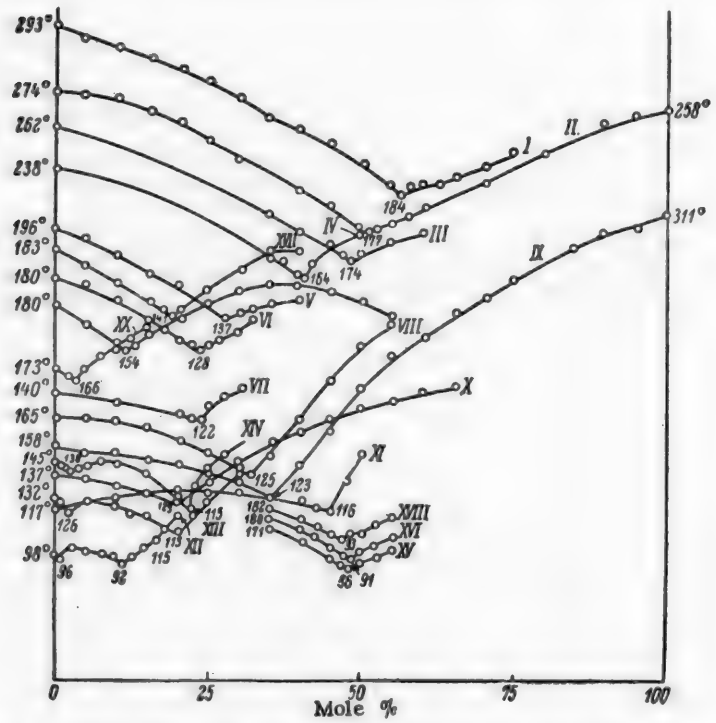

Fig. 4. Internal sections of the irreversible-reciprocal system Na, K ‖ HCOO, CNS.

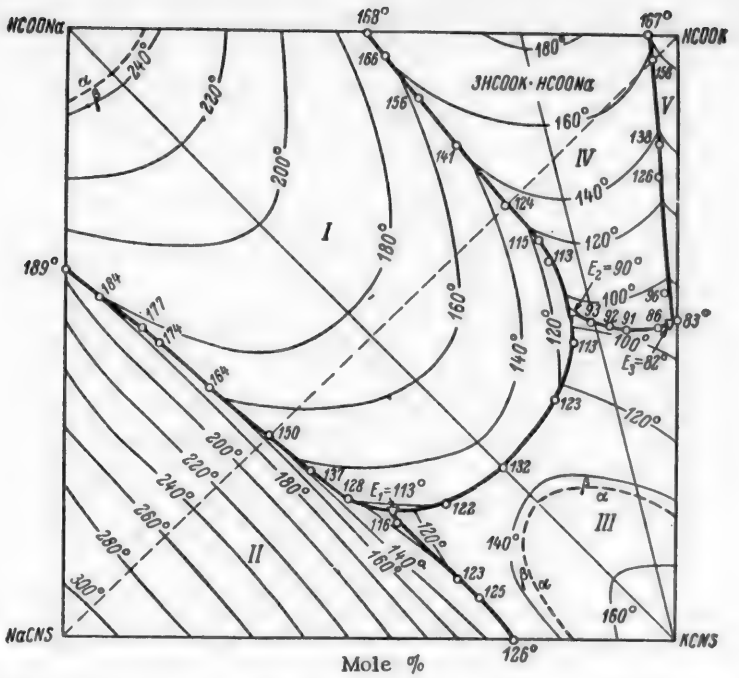

Fig. 5. Projection of the space diagram of the irreversible-reciprocal system Na, K ‖ HCOO, CNS on a composition square.

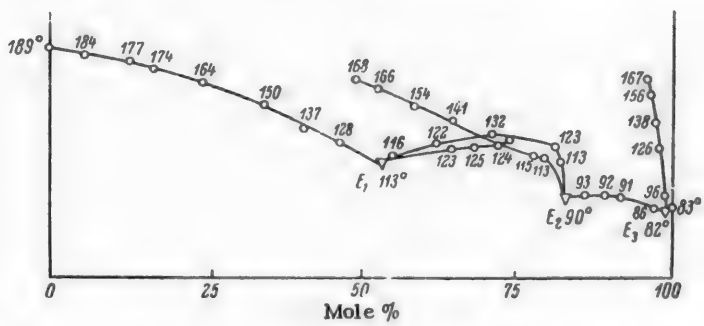

Fig. 6. Projection of lines of congruent crystallization on the NaCNS-KCNS side.

Diagonal Sections

Two arms of the melting point curve of the stable diagonal cross-section HCOONa-KCNS intersect in a eutectic point at 132° and 71.5% KCNS (Table 2, Fig. 2).

The metastable section NaCNS-HCOOK passes through four fields: 1) NaCNS, 2) HCOONa, 3) 3HCOOK · HCOONa, 4) HCOOK. The four branches of the melting point curve intersect at three points – at 150° and 34% HCOOK, 124° and 72% HCOOK, and 156° and 96.4% HCOOK (Table 2, Fig. 2).

Internal Section

For demarcation of the crystallization fields of the components and compounds of the system and for locating the three invariant points, 20 sections were drawn. The positions of the sections are shown in Fig. 3. Experimental data relating to the sections are shown in Fig. 4.

Crystallization Surface of the System

A projection of the space diagram of the reciprocal system on a composition square is shown in Fig. 5. The liquidus surface consists of five fields.

The	HCOONa	field occupies	. . .	45.82%	of the	liquidus	surface
"	NaCNS	" "	. . .	23.98	" "	"	"
"	KCNS	" "	. . .	15.55	" "	"	"
"	3HCOOK · HCOONa	" "	. . .	13.75	" "	"	"
"	HCOOK	" "	. . .	0.90	" "	"	"

In the stable diagonal section HCOONa–KCNS and the section starting from the pole of the compound 3HCOOK · HCOONa, the liquidus surface divides into three phase triangles: 1) NaCNS–HCOONa–KCNS which corresponds to the ternary eutectic point E, at 113° and 21% HCOONa, 53% KCNS and 26% NaCNS; 2) HCOONa–KCNS–3HCOOK · HCOONa with a ternary eutectic point E_2 at 90° and 16% HCOONa, 45.5% KCNS and 38.5% HCOOK; 3) 3HCOOK · HCOONa–KCNS–HCOOK with a ternary eutectic point E_3 at 82° and 0.5% HCOONa, 57.5% HCOOK and 42% KCNS.

In order to define the three invariant points accurately a projection of the lines of congruent crystallization on the NaCNS–KCNS side (Fig. 6) was constructed.

In conclusion we consider it a pleasant duty to express our thanks to A. G. Bergman.

SUMMARY

1. The binary system KCNS–HCOOK and the reciprocal system from sodium and potassium formates and thiocyanates have been investigated for the first time, by the visual-polythermal method.

2. The tendency of the exchange reaction to move in the direction of the formation of the stable pair of salts HCOONa and KCNS is in agreement with the calculated heat effect of the reaction of 4.00 kcal/equiv.

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THE IRREVERSIBLE-RECIPROCAL SYSTEM FROM SODIUM AND POTASSIUM ACETATES AND PROPIONATES

N. M. Sokolov and E. I. Pochtakova

The direction in which the interchange reaction between the sodium and potassium salts of organic acids proceeds in melts has not as yet been investigated. Among the large number of reciprocal systems on which there are data in the literature there is no system consisting of salts of organic acids. The present system is the first link in a chain of systems the general purpose of investigation of which consists in the establishment of the connection between the direction of the interchange reaction and the structure of the salt radicals.

Of the component salts of our system sodium acetate has been studied most, potassium acetate least and the propionates have been little studied.

According to the data in the literature the melting point of sodium acetate lies within the limits of 319-337° [1-7]; that of potassium acetate within the limits of 292-302° [2, 4, 8-10], the melting point of sodium propionate was determined by one of us [6] to be 298°; for potassium propionate it was known only that it melts above 300° [11]. All the salts melt without decomposition and are thermally stable up to 390°. Vorlender [12] who noticed a solidification of the salts, discovered the existence of polymorphic transformations in the case of sodium and potassium propionates, but these were not observed in the case of the acetates of these metals. Somewhat later, A. Baskov [2] investigated the binary system from potassium and sodium acetates by the differential-thermal analysis method, but polymorphism was not observed in the original salt. G. G. Diogenov [7] in an investigation of the reciprocal system from lithium and sodium acetates and nitrates obtained a sharp inflection in the sodium acetate melting-point curves, both in the binary systems and within the reciprocal systems, at 323°; on the basis of this he concluded that sodium acetate exists in two modifications, α and β, at this temperature. However, investigation by means of a differential thermocouple showed that no transformation occurs at this temperature; it takes place at 254° [4]. Other investigators have found no inflections in the sodium acetate curves at 323° [4, 6]. One of us, by the differential-thermal analysis method [13], found polymorphic transformations in sodium propionate at 77°, 195°, 217° and 287°, and in potassium propionate at 330°.

EXPERIMENTAL

For this work C. P. preparations of the acetates were taken; the propionates were synthesized by a method described earlier [6] starting from the acids and the C. P. carbonates. A commercial preparation of propionic acid was preliminarily purified by redistillation and the propionates obtained were recrystallized from butanol. The melting points of the salts used were: sodium acetate 331°, potassium acetate 301°, sodium propionate 298° and potassium propionate 365°.

The investigation was carried out by the visual-polythermal method in the usual manner. Compositions in the tables are given in molar percentages.

Binary Systems

1. The system C_2H_5COONa–C_2H_5COOK was investigated for the first time. Three branches of the melting point curve intersect in two eutectic points at 288° and 312°, at 8 and 66% potassium propionate. The composition of the compound is $2C_2H_5COONa \cdot 3C_2H_5COOK$.

TABLE 1

Binary Systems

$C_2H_5COO \parallel Na$, K		$CH_3COO, C_2H_5COO \parallel K$		$CH_3COO \parallel Na$, K		$CH_3COO, C_2H_5COO \parallel Na$	
C_2H_5COOK (%)	temp. init. crystallization	C_2H_5COO (%)	temp. init. crystallization	CH_3COOK (%)	temp. init. crystallization	C_2H_5COONa (%)	temp. init. crystallization
	298°	0	301°	0	331°	0	331°
5	292	5	310	5	322	5	326
7.5	290	10	311	10	315	10	322
8	288	15	312	15	307	15	314
10	294	20	317	20	299	20	311
15	303	25	320	25	291	25	307
20	307	30	322	30	282	30	303
25	310	35	328	35	273	35	301
30	312	40	331	40	264	40	298
35	315	45	334	42.5	258	45	300
40	316	50	339	45	254	50	299
45	317	55	342	47.5	247	55	299
50	317	60	346	50	244	60	298
55	318	65	348	52.5	238	65	297
60	319	70	352	53.5	235	70	296
66	312	75	356	55	238	75	295
67.5	313	80	358	57.5	238	85	294
70	317	85	362	60	241	90	293
75	324	90	364	61.5	240	95	291
85	340	95	365	62.5	242	97.5	295
90	348	100	365	65	246	100	298
95	358			67.5	251		
100	365			70	255		
				75	263		
				80	272		
				85	282		
				90	290		
				95	298		
				100	301		

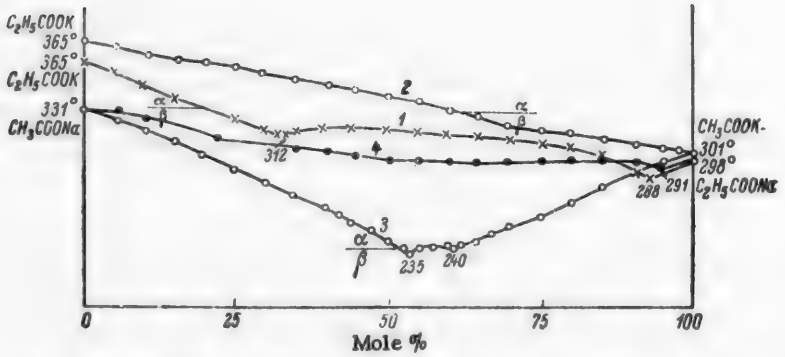

Fig. 1. Melting point diagram of the binary systems: 1) C_2H_5COOK–C_2H_5COONa; 2) C_2H_5COOK–CH_3COOK; 3) CH_3COOK–CH_3COONa; 4) CH_3COONa–C_2H_5COONa.

2. The system C_2H_5COOK–CH_3COOK was investigated for the first time. Here a continuous series of solid solutions occurs with no extremum on the melting point curve.

3. The system CH_3COONa–CH_3COOK was first described as a continuous series of solid solutions with a minimum [2], and then as a system with a eutectic [4]. According to our data a compound is formed in this case, of the probable composition – $3CH_3COOK \cdot 2CH_3COONa$. Three branches of the melting point curve intersect in a eutectic point at 235° and 53.5% potassium acetate and in a transition point at 240° and 61.5% potassium acetate.

TABLE 2

Diagonal Sections

C_2H_5COOK–CH_3COONa (stable section)		C_2H_5COONa–CH_3COOK (metastable section)	
CH_3COONa (%)	temperature of initial crystallization	CH_3COOK (%)	temperature of initial crystallization
0	365°	0	298°
2.5	365	2.5	291
5	364	5	287
10	353	6	285
15	344	7.5	284
20	330	10	283
25	317	15	279
30	304	17.5	273
35	291	20	272
40	276	22.5	271
45	260	25	266
50	247	27.5	262
52.5	244	30	257
55	240	32.5	252
57	236	35	249
57.5	238	36	246
60	245	37.5	245
65	249	40	243
75	275	42.5	242
80	287	43	240
85	296	45	242
90	308	50	245
95	321	52.5	247
97.5	326	55	248
100	331	57.5	250
		60	252
		62.5	257
		65	259
		67.5	262
		70	264
		75	269
		80	278
		85	285
		90	289
		95	293
		97.5	295
		100	301

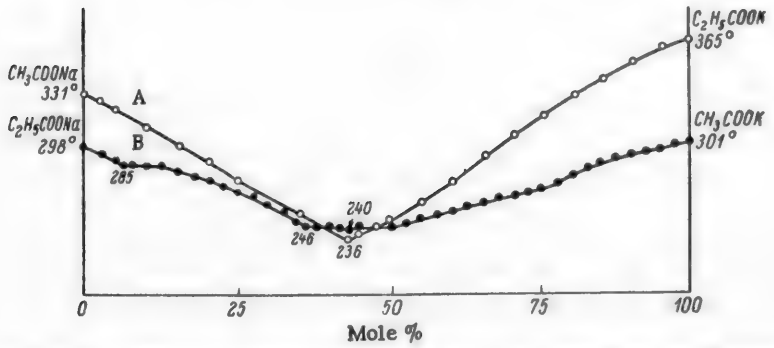

Fig. 2. Diagonal sections of the systems: A) stable diagonal section; B) metastable diagonal section.

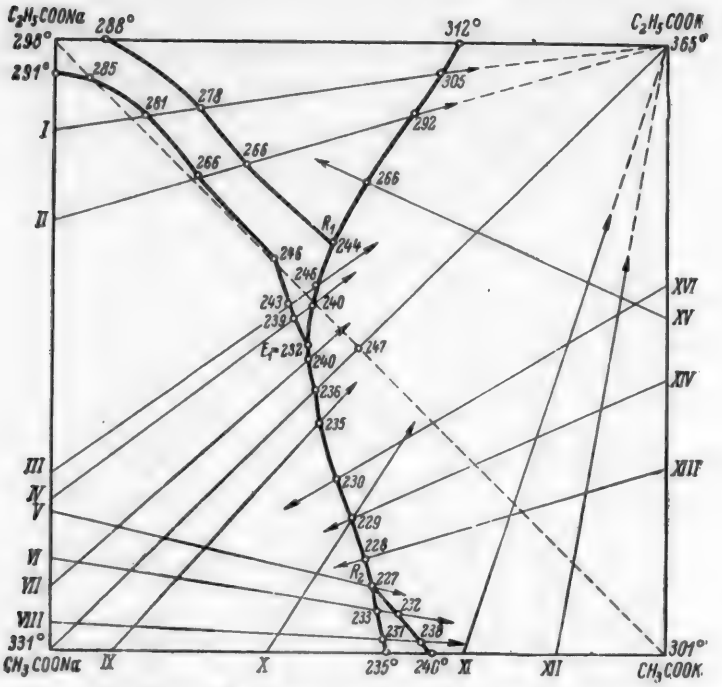

Fig. 3. Positions of the internal sections of the reciprocal system Na, K ‖ CH_3COO, C_2H_5COO.

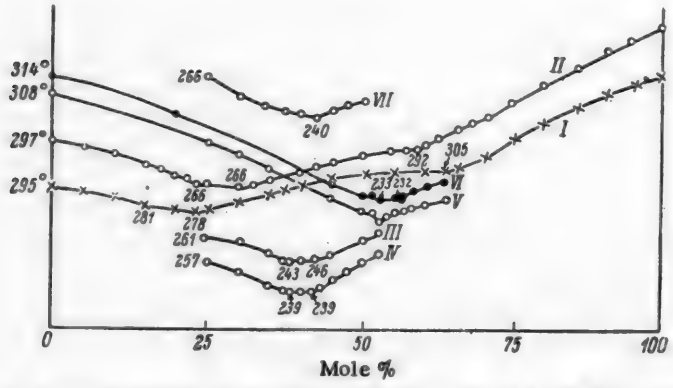

Fig. 4. Internal sections of the reciprocal system Na, K ‖ CH_3COO, C_2H_5COO.

4. The system CH_3COONa–C_2H_5COONa was studied by us for the first time. Two branches of the melting point curve intersect at 291° and 95% sodium propionate.

The melting point curves of the binary systems, constructed from the data in Table 1, are depicted in Fig. 1.

Diagonal Sections

The stable diagonal section of C_2H_5COOK–CH_3COONa has two melting point branches that intersect in a eutectic point at 236° and 57% sodium acetate (Table 2, Fig. 2). The metastable diagonal section of C_2H_5COONa–CH_3COOK passes through four fields: twice through the C_2H_5COONa field, the CH_3COONa field and the field of the solid solutions. In conformity with this the melting-point curve consists of four branches

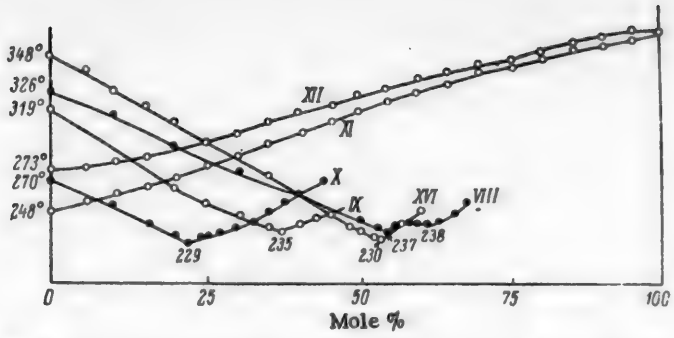

Fig. 5. Internal sections of the reciprocal system Na, K ‖ CH_3COO, C_2H_5COO.

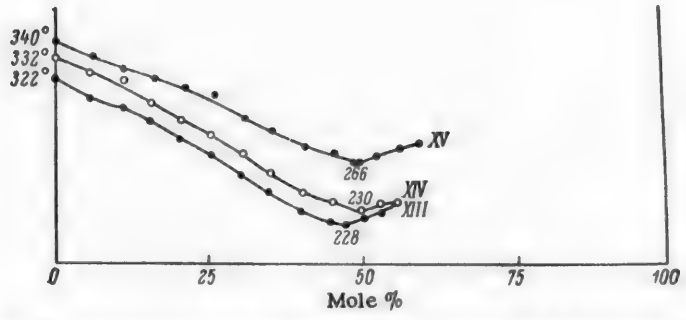

Fig. 6. Internal sections of the reciprocal system Na, K ‖ CH_3COO, C_2H_5COO.

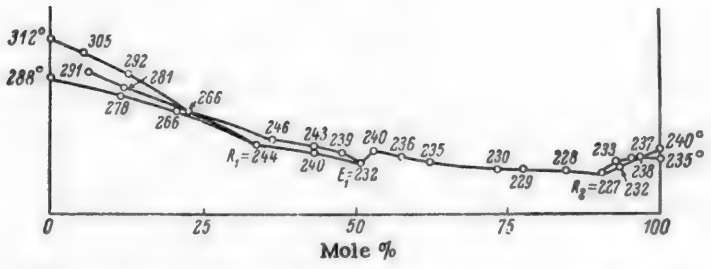

Fig. 7. Projection of the lines of congruent crystallization on the C_2H_5COONa–CH_3COONa side.

that intersect in three points: at 285° and 6% potassium acetate, at 246° and 36% potassium acetate and at 240° and 43% potassium acetate (Table 2, Fig. 2).

Internal Sections

For demarcation of the crystallization fields of the components of the system and of the compounds, and for finding the ternary invariant points, 16 ternary sections were studied, the directions of which are shown in Fig. 3, and the melting point curves of the sections are depicted in Figs. 4-6.

A projection of the lines of congruent crystallization on the C_2H_5COONa–CH_3COONa side are given in Fig. 7, and a projection of the space diagram on a composition square is given in Fig. 8.

The liquidus surface of the system consists of five fields:

The solid solutions		field occupies	. . .	48.25%	of	the	liquidus	surface
"	CH_3COONa	" "	. . .	36.20%	"	"	"	"
"	$2C_2H_5COONa \cdot 3C_2H_5COOK$	" "	. . .	10.40%	"	"	"	"
"	C_2H_5COONa	" "	. . .	4.25%	"	"	"	"
"	$2CH_3COONa \cdot 3CH_3COOK$	" "	. . .	0.90%	"	"	"	"

Diagonal system. The compounds that are formed in the binary systems do not show an effect on the direction of the exchange reaction. Their fields taper off to the inside of the diagram of the reciprocal system; they end in a transition point and do not take part in the triangulation. The stable diagonal C_2H_5COOK–CH_3COONa system is divided into two ternary systems: 1) CH_3COONa–C_2H_5COONa–C_2H_5COOK and 2) CH_3COONa–CH_3COOK–C_2H_5COOK. In the first system there is a ternary eutectic point E at 232° and 50.5% CH_3COONa, 42% C_2H_5COOK and 7.5% C_2H_5COONa and a transition point R_1 at 244° and 33.5% CH_3COONa, 45% C_2H_5COOK and 21.5% C_2H_5COONa. In the second system there is a transition point R_2 at 227° and 11% C_2H_5COOK, 47% CH_3COONa and 42% CH_3COOK.

We consider it a pleasant duty to thank A. G. Bergman for his valuable advice during the course of this work.

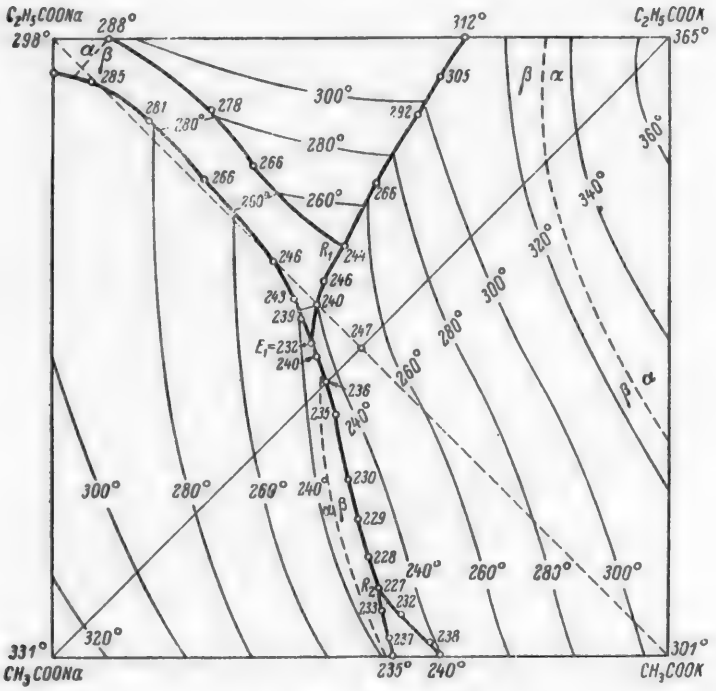

Fig. 8. Projection of the space diagram of the reciprocal system Na, K ‖ CH_3COO, C_2H_5COO on a composition square.

SUMMARY

1. The binary systems CH_3COO, C_2H_5COO ‖ K; CH_3COO, C_2H_5COO ‖ Na and C_2H_5COO ‖ Na, K have been studied for the first time.

2. Investigation of the binary system from sodium and potassium acetates, in which we established the occurrence of complex formation, has been repeated.

3. The liquidus surface of the irreversible-reciprocal system CH_3COO, C_2H_5COO ‖ Na, K has been studied.

4. The equilibrium in the system is displaced towards the side of the higher melting components.

5. It is not possible to check the conformity of the direction of the reaction by means of the calculated heat effect because of the absence of data on the heats of formation of the propionates.

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** In Russian.

THE TERNARY SYSTEM
FROM LITHIUM AND SODIUM PROPIONATES AND NITRATES

N. M. Tsindrik and N. M. Sokolov

This system is the next link in the chain of systems that are being investigated for the purpose of establishing the relationship between the direction of the exchange reaction between lithium salts of organic acids and sodium nitrate, and the length of the carbon chain in the acid radical.

It was shown earlier that in analogous systems with formates and acetates that the equilibrium is displaced toward the sodium nitrate and lithium fatty-acid-salt side [1, 2]. In the system with acetates the equilibrium is markedly displaced. The present system should provide an answer to the question as to whether the shift increases regularly.

In contrast to the nitrates lithium and sodium propionates have been little studied. Thus, for example, their melting points were first determined by one of us quite recently [4]. Vorlender [5], without stating the temperatures, considered that sodium propionate undergoes polymorphic transformations. One of us found polymorphic transformations for sodium propionate at 77, 195, 217 and 287° [3].

All the salts of the system being studied melt without decomposition. On overheating, the propionates darken and decompose with evolution of gases and in mixtures with nitrates the decomposition is accompanied by ignition.

EXPERIMENTAL

The system was investigated by the visual-polythermal method according to the generally accepted technique. Commercial preparations of lithium and sodium nitrates were used. C. P. sodium nitrate was purified according to Laiti [6] and "Pure for Analysis" lithium nitrate was twice recrystallized. Lithium and sodium propionates were prepared synthetically by the method described previously [4]. The propionates so obtained were recrystallized from butanol. The initial components of the system had the following melting points; sodium nitrate 308°, lithium nitrate 256°, sodium propionate 298°, lithium propionate 329°.

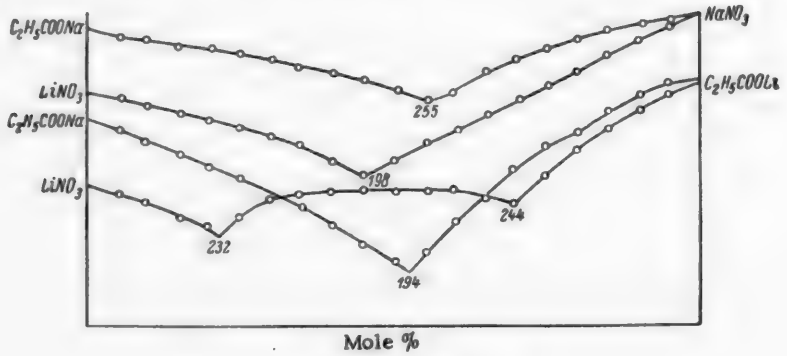

Fig. 1. Binary systems.

TABLE 1

Binary Systems

$LiNO_3$–$NaNO_3$		$LiNO_3$–C_2H_5COOLi		C_2H_5COOLi–C_2H_5COONa		C_2H_5COONa–$NaNO_3$	
$NaNO_3$ (mole %)	temp.	C_2H_5COOLi (mole %)	temp.	C_2H_5COONa (mole %)	temp.	$NaNO_3$ (mole %)	temp.
0	256°	0	256°	0	329°	0	298°
5	250	5	252	5	322	5	294
10	242	10	246	10	316	10	291
15	236	15	240	15	304	15	287
20	230	20	234	20	292	20	284
25	224	21.5	232	25	278	25	282
30	216	22.5	234	30	262	30	280
35	210	25	238	35	246	35	276
40	204	30	244	40	226	40	273
45	198	35	248	42.5	218	45	269
50	208	40	252	45	206	50	264
55	219	45	253	47.5	196	55	258
60	230	50	252	48	194	60	260
65	240	55	252	50	198	65	270
70	250	60	252	52.5	204	75	280
80	270	65	250	55	212	80	286
90	290	70	244	57.5	216	90	298
100	308	75	266	60	224	95	302
		80	280	70	248	100	308
		90	307	80	266	—	—
		100	329	90	282	—	—
				100	298	—	—

TABLE 2

Diagonal Sections

$LiNO_3$–C_2H_5COONa				C_2H_5COOLi–$NaNO_3$			
C_2H_5COONa (mole %)	temp.	C_2H_5COONa (mole %)	temp.	$NaNO_3$ (mole %)	temp.	$NaNO_3$ (mole %)	temp.
0	256°	37.5	260°	0	329°	60	284°
2.5	250	40	270	5	318	70	284
5	245	42.5	280	10	304	80	284
10	230	45	282	15	286	90	290
12.5	224	50	284	20	270	100	308
14.5	216	55	284	22	264		
15	218	60	282	25	274		
17.5	224	65	276	30	284		
20	228	70	260	40	284		
22.5	228	72.5	260	50	284		
25	230	75	240				
27.5	226	77.5	234				
29	224	80	244				
30	232	85	260				
32.5	242	90	270				
35	252	100	298				

Binary Systems (Table 1, Fig. 1)

The system $LiNO_3$–C_2H_5COOLi was investigated for the first time. The melting point curve consists of three branches – the lithium propionate, compound $2C_2H_5COOLi \cdot 3LiNO_3$ and lithium nitrate branches. The branches intersect in eutectic points corresponding to 70 and 22.5% lithium propionate and melting points of 244 and 232° respectively.

The system $C_2H_5COOLi - C_2H_5COONa$. The melting point curve consists of two branches intersecting at 194° and 48% sodium propionate.

The system $C_2H_5COONa - NaNO_3$. The eutectic point corresponds to 56% sodium nitrate and 255° [4].

The system $NaNO_3 - LiNO_3$ recurs in all the ternary reciprocal systems investigated by us from lithium and sodium salts of fatty acids and the nitrates of these metals. The system has a eutectic containing 45% sodium nitrate of m. p. 198°.

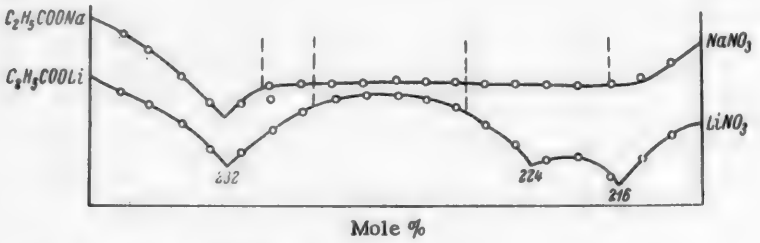

Fig. 2. Diagonal Sections.

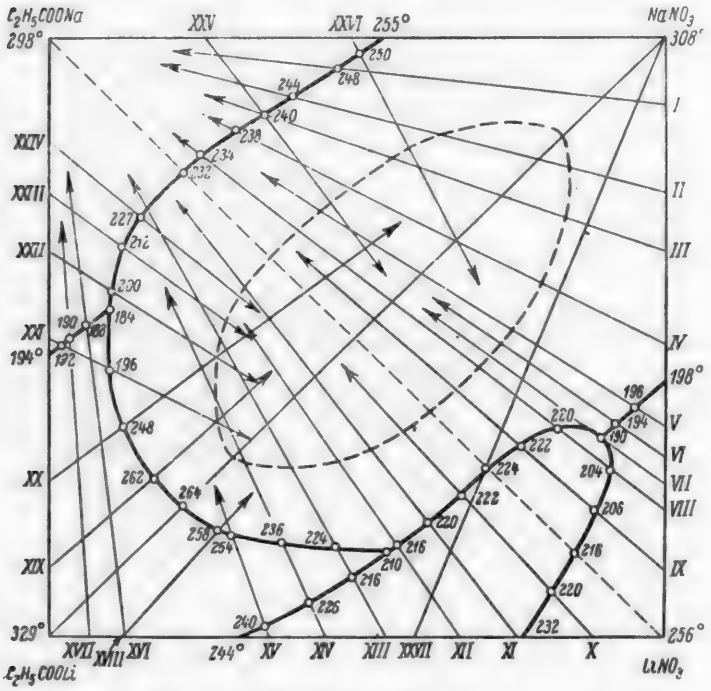

Fig. 3. Positions of the internal sections.

Diagonal Sections (Table 2, Fig. 2)

The diagonal section $C_2H_5COOLi - NaNO_3$ has a eutectic at 22% sodium nitrate and 264°. On this section stratification was observed from 29 to 85% sodium nitrate.

The diagonal system $LiNO_3 - C_2H_5COONa$ has four primary crystallization branches – the $LiNO_3$, compound $2C_2H_5COOLi \cdot 3LiNO_3$, the interchange product and C_2H_5COONa. The inflection points of the branches correspond

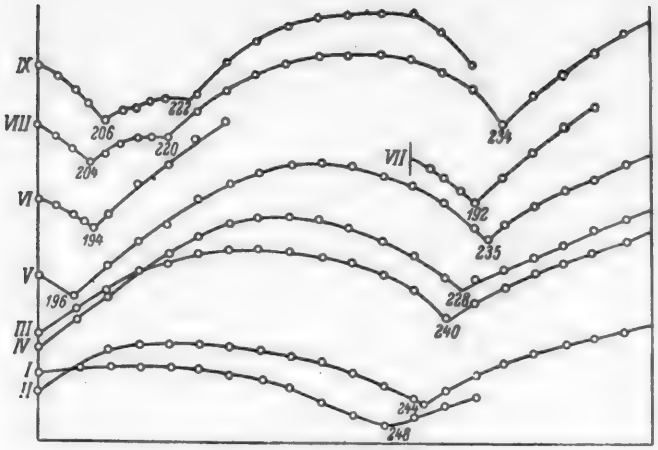

Fig. 4. Internal sections I-IX.

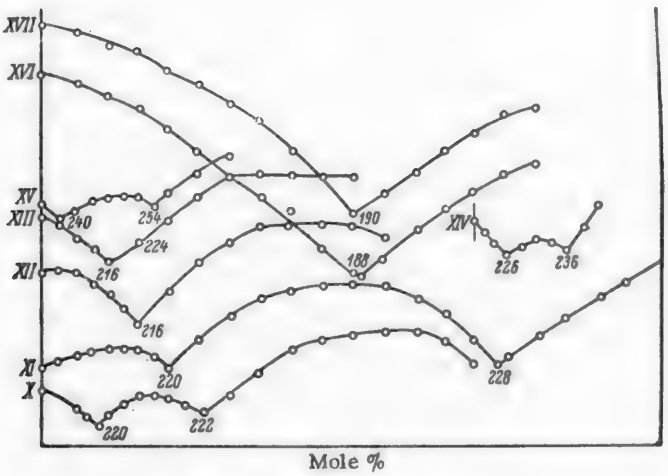

Fig. 5. Internal sections X-XVII.

TABLE 3

Point	Temperature	Composition of the eutectics (in mole %)			
		$NaNO_3$	$LiNO_3$	C_2H_5COOLi	C_2H_5COONa
E_1	184°	7.5	—	47.5	45
E_2	210	14	38.5	47.5	—
E_3	190	32.5	57.5	10	—

to the coordinates: 14% C_2H_5COONa and 216°, 29% C_2H_5COONa and 224°, 78% C_2H_5COONa and 232°. Stratification was observed in the interval from 38 to 62.5% C_2H_5COONa.

For construction of composition diagrams of the ternary system, 27 internal sections of it were investigated, the directions of which are shown in Fig. 3, and the data obtained are presented graphically in Figs. 4-6.

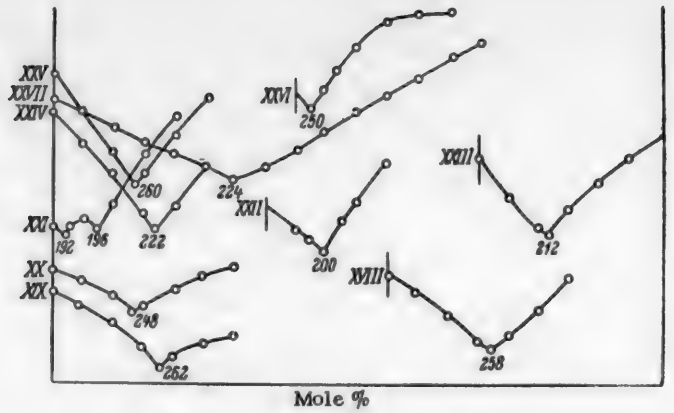

Fig. 6. Internal sections XVIII-XXVII.

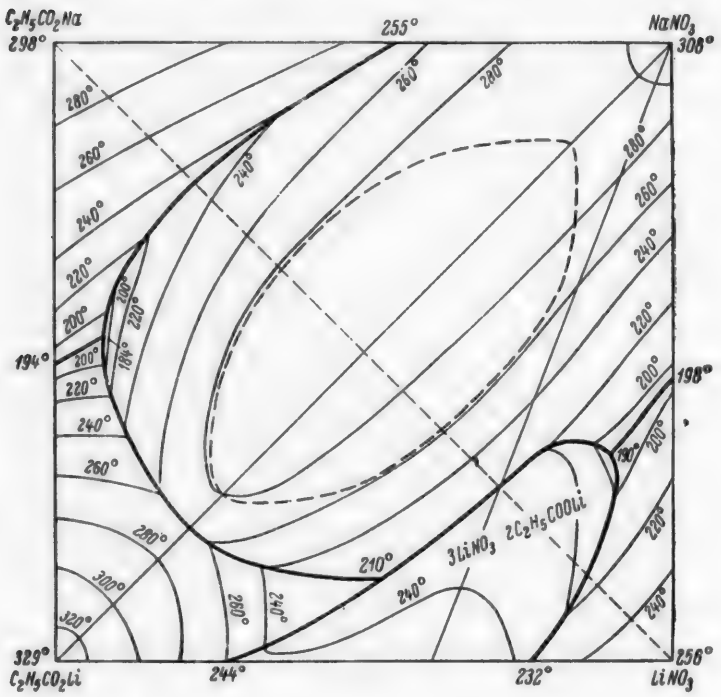

Fig. 7. Ternary reciprocal system.

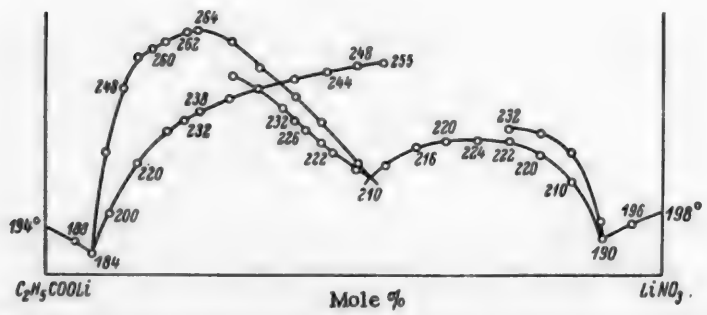

Fig. 8. Projection of invariant points and curves of congruent crystallization of the ternary system Li, Na || C_2H_5COO, NO_3 on the $LiNO_3$–C_2H_5COOLi side.

Study of the binary systems and the diagonal and internal sections enabled a projection of the space diagram to be constructed on a composition square (Fig. 7).

The liquidus surface of the system consists of five fields. The areas of the fields in percentages of the total are: $LiNO_3$ field 5.07, C_2H_5COOLi field 12.17, C_2H_5COONa field 12.29, the field of the compound 10.74, and the $NaNO_3$ field 59.73. The stratification field is in the $NaNO_3$ field and forms 36.82% of its area.

The system is divided at the $NaNO_3$ apex by the stable diagonal section C_2H_5COOLi–$NaNO_3$ and the section starting from the pole of the compound $2C_2H_5COOLi \cdot 3LiNO_3$, into three phase triangles:

1) $NaNO_3$–C_2H_5COONa–C_2H_5COOLi,
2) $NaNO_3$–C_2H_5COOLi–$2C_2H_5COOLi \cdot 3LiNO_3$ and
3) $NaNO_3$–$2C_2H_5COOLi \cdot 3LiNO_3$–$LiNO_3$.

The positions of the eutectic points are given in Table 3.

The positions of the invariant points and the curves of congruent crystallization are given in the form of projections on the $LiNO_3$–C_2H_5COOLi side in Fig. 8.

As the results obtained show, in the system investigated as in the systems with formates and acetates, the equilibrium is displaced toward the side of the lithium salt of the fatty acid and sodium nitrate. The nature and extent of the displacement give grounds for considering that there is possibly some regular relationship here. This in its turn involves the question of further investigation in this direction.

SUMMARY

1. The binary systems $LiNO_3$–C_2H_5COOLi and C_2H_5COONa–C_2H_5COOLi have been investigated for the first time.

2. A melting point diagram of the ternary reciprocal system from lithium and sodium propionates and nitrates has been obtained.

3. The equilibrium in the ternary system is displaced toward the lithium propionate and sodium nitrate side: with increasing numbers of carbon atoms in the fatty acid radical the displacement of the equilibrium increases in systems consisting of formates, acetates or propionates with lithium and sodium nitrates.

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COMPLEX COMPOUNDS OF STANNIC CHLORIDE AND BROMIDE WITH UREA

E. Sh. Iarmukhamedova and T. N. Sumarokova

In a systematic study of the complex compounds of quadrivalent tin with organic compounds containing nitrogen and oxygen we found that thiourea reacts with stannic chloride and bromide with the formation of a complex compound of the composition $SnX_4 \cdot 2(NH_2)_2CS$ [1]. It seemed of interest to us to study the behavior of urea with respect to the quadrivalent tin halides. Taking into consideration the similarity between thiourea and urea we felt that the latter should form compounds of analogous composition with stannic chloride and bromide.

EXPERIMENTAL

Stannic chloride was purified by multiple redistillation; the fraction boiling at 109° (690 mm) was collected in an ampoule which was then sealed. Stannic bromide was purified in a similar manner. The fraction boiling at 196° (700 mm) was collected in an ampoule; m. p. 29.2°. Acetic acid was fractionally frozen out and then redistilled, the fraction boiling at 113.5° (693 mm) was collected in an ampoule; m. p. 16.57°. Urea was purified by recrystallization from absolute alcohol; m. p. 132.7°.

1. The complex compound of stannic chloride with urea was prepared by direct reaction between stannic chloride and urea in the absence of a solvent. Stannic chloride was mixed with urea in the ratios 1 mole of $SnCl_4$ to 1 mole of $(NH_2)_2CO$ and 1 mole of $SnCl_4$ to 2 moles of $(NH_2)_2CO$. No visible change was observed by the action of stannic chloride on urea at room temperature. However, when the mixture was gently heated, a very vigorous reaction set in and a colorless, crystalline precipitate was formed. On mixing stannic chloride with urea in the ratio 1:1 a precipitate separated and some unreacted stannic chloride remained in the flask. The 1:2 mixture crystallized completely. The solid products obtained were transferred to a glass filter and thoroughly washed with hot benzene. After drying in a vacuum desiccator over P_2O_5 they were analyzed for their tin and chlorine contents.

The results of analysis of the product that separated from the 1:2 mixture are given below.

Found %: Sn 31.80, 31.67, 31.89, 31.83; Cl 37.40, 37.31, 37.18, 37.10. $SnCl_4 \cdot 2(NH_2)_2CO$. Calculated %: Sn 31.18; Cl 37.25.

The analysis shows that the tin and chlorine contents of the product are in good agreement with that calculated for a compound of 1:2 composition.

The following results of analysis of the precipitate from the 1:1 mixture were obtained.

Found %: Sn 30.20, 30.29, 30.32, 30.38; Cl 36.42, 36.47. $SnCl_4 \cdot (NH_2)_2CO$. Calculated %: Sn 37.02; Cl 44.23.

The analysis shows that the tin and chlorine content of the product do not correspond to the compound $SnCl_4 \cdot (NH_2)_2CO$ but to the formula $SnCl_4 \cdot 2(NH_2)_2CO$.

The results of analysis of the precipitate formed on addition of stannic chloride to a solution of urea in acetic acid (1 mole of stannic chloride to 4 moles of urea) are given below.

Found %: Sn 30.23, 30.61. $SnCl_4 \cdot 4(NH_2)_2CO$. Calculated %: Sn 23.70.

These figures also indicate that the tin and chlorine contents in the product correspond to the compound $SnCl_4 \cdot 2(NH_2)_2CO$.

It is therefore evident that on mixing stannic chloride with urea in various stoichiometric proportions, only one compound, $SnCl_4 \cdot 2(NH_2)_2CO$, is formed.

We also made a cryoscopic study of the system $SnCl_4$–$2(NH_2)_2CO$ in acetic acid. The variation of the melting point depression with composition, expressed as moles per cent, is shown in Figure 1.

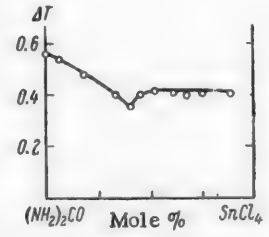

Fig. 1. Cryoscopic titration of a solution of urea in acetic acid with stannic chloride.

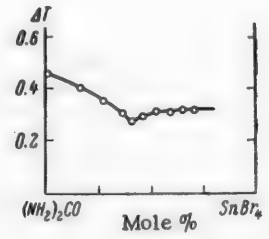

Fig. 2. Cryoscopic titration of a solution of urea in acetic acid with stannic bromide.

It is seen from the graph that on addition of stannic chloride to a solution of urea in CH_3COOH, the magnitude of the depression falls to an equivalent point, then rises a little and finally becomes constant. The constancy of the depression is brought about by the limited solubility of stannic chloride in acetic acid. The equivalent point falls at 33 mole % $SnCl_4$, indicating the formation of a complex compound of stannic chloride and urea of the composition $SnCl_4 \cdot 2(NH_2)_2CO$.

2. The complex compound of stannic bromide and urea was prepared by direct interaction of the components in the absence of a solvent. Stannic bromide was mixed with urea in the proportions 1 mole of $SnBr_4$ to 1 mole of $(NH_2)_2CO$ and 1 mole of $SnBr_4$ to 2 moles of $(NH_2)_2CO$. The reaction between stannic bromide and urea was accompanied by considerable evolution of heat. The 1:2 mixture crystallized completely in the form of a yellow material; in the 1:1 mixture, in addition to the compound formed, a certain amount of unreacted stannic bromide remained, which crystallized out at room temperature in the form of colorless, crystalline inclusions.

The following are the results of analysis of the product obtained from the 1:2 mixture.

Found %: Sn 20.96, 21.00, 21.20; Br 57.51, 57.16, 57.73. $SnBr_4 \cdot 2(NH_2)_2CO$. Calculated %: Sn 21.25; Br 57.23.

From the above figures it is seen that the reaction product from stannic bromide and urea is a compound corresponding to the formula $SnBr_4 \cdot 2(NH_2)_2CO$.

On analysis of the product that separated from the 1:1 mixture the following results were obtained.

Found %: Sn 21.75, 21.54, 21.37, 21.72, 21.36; Br 57.00, 56.66, 56.54, 57.41, 57.39. $SnBr_4 \cdot (NH_2)_2CO$. Calculated %: Sn 23.81; Br 64.13.

The analysis of the precipitate shows that the tin and bromine contents do not correspond to the compound $SnBr_4 \cdot (NH_2)_2CO$, but to the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

The results of a cryoscopic study of the system $SnBr_4$–$(NH_2)_2CO$ in acetic acid are given in Fig. 2 in the form of a graph of melting point depression against composition. On addition of stannic bromide to a solution of urea in CH_3COOH the depression falls to a point of equivalence, then rises a little, after which further addition of stannic bromide does not cause any change in the depression. The constancy of the depression as in the case of stannic chloride, is caused by the limited solubility of stannic bromide in CH_3COOH. The inflection point in the curve falls at 33 mole % $SnBr_4$, indicating the formation of the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

Thus, the results of the cryoscopic study of the system $SnBr_4$–$(NH_2)_2CO$, and also the results of analysis of the products, indicate the existence of the compound $SnBr_4 \cdot 2(NH_2)_2CO$.

SUMMARY

The complex compounds of stannic chloride and bromide with urea, $SnCl_4 \cdot 2(NH_2)_2CO$ and $SnBr_4 \cdot 2(NH_2)_2CO$, have been prepared.

These complex compounds are crystalline substances, stable in air, and have poor solubility in organic solvents.

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REDUCTION OF LIMONENE MONOXIDE WITH LITHIUM ALUMINUM HYDRIDE

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The catalytic hydrogenation of α-oxides of the terpene series to the corresponding alcohols, as was found by one of us [1], is very difficult to achieve. In such cases where this reaction is accomplished under more rigorous conditions, it is accompanied by a number of secondary processes. Thus, on hydrogenation of the oxides of Δ^2-menthene and Δ^1-menthene (carvomenthene) in acetic acid in the presence of hydrated palladium oxide, in addition to the alcohols (the normal products of hydrogenation) p-menthane is obtained and also partial isomerization of the oxides to the ketones takes place; moreover the acetates of the corresponding glycols are also formed. In the case of carvomenthene oxide, the amount of secondary products is as much as 67%. A more convenient method for the conversion of terpene α-oxides to the alcohols is that of reduction of the oxides with lithium aluminum hydride, since this reaction is not usually accompanied by secondary processes.

The material chosen for the present research is limonene monoxide (oxido-1,2-p-menthane-8,9), first synthesized by N. A. Prilezhaev [2]. On reduction of this oxide with lithium aluminum hydride the alcohols, D-neodihydrocarveol of high asymmetric purity ($[\alpha]_D$ + 32.8°) and β-terpineol of m. p. 31-31.5°, are formed exclusively. We characterized the two alcohols by means of suitable derivatives: D-neodihydrocarveol hydrate of m. p. 156-156.5° and β-terpineol phenylurethane of m. p. 84-85°. In addition we recorded the Raman spectra of the alcohols. The spectrum of D-neodihydrocarveol is published for the first time. As regards the spectrum of β-terpineol reported in the literature [3], this relates to a mixture of β- and α-terpineol [4]; α-terpineol was not present as an impurity in our sample of β-terpineol.

Our results indicate that the oxide ring of limonene monoxide on reduction opens simultaneously in the two possible directions. On the basis of the magnitude of the optical activity of the mixture of alcohols obtained from the reduction, and also from the ratios of the characteristic spectral lines* in the spectrum of the mixture of alcohols, the conclusion can be drawn that the two alcohols are formed in approximately equal quantities. The results of direct fractionation of the reduction products confirms this view. Excess of reducing agent and further heating of the reaction mixture after mixing of the reagents is complete has practically no effect on the yield of the alcohols.

After our investigation had been completed we became acquainted with the paper of Holub, Herout and Sorm [6], dealing with the synthesis of α-bisabolol. In this work, as one of the intermediate compounds, the reduction product of limonene monoxide with lithium aluminum hydride was used, and the authors considered this to be β-terpineol. The authors of this paper evidently did not take account of the fact that neodihydrocarveol is formed in addition to β-terpineol on reduction of limonene monoxide.

EXPERIMENTAL

Preparation of limonene monoxide. D-limonene (b. p. 59-60° at 11 mm, d^{20}_4 0.8466, $n^{20}D$ 1.4726, $[\alpha]_D$ + 126°), which was used for the preparation of the monoxide, was isolated from caraway oil. Limonene monoxide was synthesized from D-limonene by the action of peracetic acid in ethereal solution [7]. The oxide was characterized by the following constants: b. p. 110-112° at 50 mm, d^{20}_4 0.9324, $n^{20}D$ 1.4671, $[\alpha]_D$ + 65.5°.

* For β-terpineol, as for a tertiary alcohol of the p-menthane series, there is a characteristic line of rocking vibration of the ring with $\Delta\nu$ 721 cm^{-1}; for neodihydrocarveol, having a hydroxyl group in the axial position on the secondary carbon atom – a line with $\Delta\nu$ 750 cm^{-1} [5].

Reduction of limonene monoxide. 175 ml of an ethereal solution of lithium aluminum hydride (8.1 g of $LiAlH_4$), prepared according to the method of Wieberg and Schmidt [8], was slowly run into 33 g of limonene monoxide dissolved in 275 ml of ether, in a current of dry nitrogen. The reaction mixture was refluxed for 2 hours, then cooled and 100 ml of water was added gradually to the mixture. The main part of the ethereal layer was poured off and the aqueous layer, with the precipitate formed, was treated with 10% aqueous sodium hydroxide solution. The milk-white liquid obtained was extracted with ether. The combined ethereal extracts were dried over potassium carbonate. The reaction product, after removal of the ether, was distilled in vacuo. 27 g (84%) of a mixture of alcohols of b. p. 110-113° at 27 mm, $n^{20}D$ 1.4772, $[\alpha]_D$ + 18.6°, was obtained.

Found %: OH 10.70, 10.53. $C_{10}H_{18}O$. Calculated %: OH 11.03.

The reduction of limonene monoxide with lithium aluminum hydride was repeated twice. In one of these experiments the reaction mixture was refluxed for 3 hours; the yield of reduction products was 75%. In the other experiment the reaction mixture, after addition of the $LiAlH_4$ solution, was allowed to stand for only 10 minutes at room temperature before treatment with water; yield 69%.

Separation of the reduction products was carried out by fractionating the mixture in vacuo through a column with an efficiency of 25 theoretical plates. Two main fractions were isolated from the fractionation of 51 g of the mixed reduction products: 1st fraction, b. p. 91-91.5° at 10 mm, 13.8 g (β-terpineol) and 2nd fraction, b. p. 117° at 32 mm, 18.7 g (D-neodihydrocarveol).

β-Terpineol

B. p. 91-91.5° at 10 mm, m. p. 31-31.5°, $[\alpha]_D$ 0.0°, d^{20}_4 0.9235, $n^{20}D$ 1.4749. Literature data [9]: b. p. 90° at 10 mm, m. p. 32-33°, d^{20}_4 0.9235, $n^{20}D$ 1.4747.

Found %: C 78.21, 78.15; H 11.86, 11.87; OH 11.21. $C_{10}H_{18}O$. Calculated %: C 77.92; H 11.68; OH 11.03.

M. p. phenylurethane 84-85°. Literature data for β-terpineol phenylurethane [9]: m. p. 85°.

D-Neodihydrocarveol

B. p. 117° at 32 mm, d^{15}_4 0.9337, $n^{20}D$ 1.4798, $[\alpha]_D$ + 32.8°. Literature data for L-neodihydrocarveol hydrate [10]: m. p. 214-215°, d^{15}_4 0.930, $n^{20}D$ 1.48016, $[\alpha]_D$ −32.5°.

Found %: C 78.12, 77.93; H 11.71, 11.80; OH 10.77. $C_{10}H_{18}O$. Calculated %: C 77.92; H 11.68; OH 11.03.

For the preparation of D-neodihydrocarveol hydrate [11] 4.2 g of D-neodihydrocarveol was shaken for 30 hours with 200 ml of 5% sulfuric acid. The precipitate formed was separated, washed with water and dried. Yield 2.6 g. After two recrystallizations from water, m. p. 156-156.5°, $[\alpha]_D$ + 40.1° (ethanol, C = 10). Literature data for L-neodihydrocarveol hydrate [11]: m. p. 158-159°, $[\alpha]_D$ −40.0°.

Raman Spectra

Spectrum of limonene monoxide. $\Delta\nu$: 240 (3), 289 (5), 323 (3), 393 (3), 502 (2), 526 (2), 556 (1), 612 (2), 674 (9), 693 (2), 757 (8), 794 (3), 841 (6), 883-900 (5), 1041 (3), 1081 (1), 1096 (2), 1119 (2), 1150 (4), 1210 (4), 1303 (5), 1423 (6), 1453 (4), 1643 (10), 2863 (5), 2922 (10), 2983 (5). (Cf. [4]).

Spectrum of the mixture of alcohols obtained on reduction of limonene monoxide. $\Delta\nu$: 278 (1), 303 (1), 340 (1), 395 (2), 444 (2), 502 (3), 539 (2), 605 (1), 723 (6), 752 (7), 797 (1?), 813 (1), 869-894 (5), 915 (1?), 948 (2), 994 (4), 1038 (4), 1076-1118 (5), 1132-1166 (8), 1211 (6), 1220 (6), 1253 (6), 1268 (6), 1434 (8), 1454 (8), 1643 (10), 2868 (4), 2925 (6), 2976 (2).

Spectrum of β-terpineol. $\Delta\nu$: 276 (1), 304 (1), 335 (1), 394 (1), 442 (1), 501 (2), 541 (1), 721 (10), 772 (2), 797 (1), 815 (1), 878 (2), 910 (1), 986-1047 (3), 1135-1169 (7), 1215 (1), 1268 (3), 1395 (1), 1432 (5), 1455 (5), 1642 (8), 2864 (2), 2925 (4), 2970 (2?).

Spectrum of D-neodihydrocarveol. $\Delta\nu$: 302 (1), 391 (1), 439 (1), 501 (1), 561 (1), 715 (1), 750 (10), 801 (1), 859 (1), 882 (2), 942 (2), 990 (2), 1036 (3), 1082 (4), 1101 (4), 1124-1165 (4), 1250 (5), 1309 (4), 1433 (6), 1453 (6), 1641 (8), 2866 (5), 2925 (6).

SUMMARY

1. It has been established that reduction of limonene monoxide with lithium aluminum hydride takes place with opening of the oxide ring in the two possible directions, with the formation of the tertiary alcohol β-terpineol and the secondary alcohol D-neodihydrocarveol.

2. The Raman spectra of β-terpineol and D-neodihydrocarveol, which has been prepared for the first time, are recorded.

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SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.